STIC Search Report
EIC 1700

STIC Database Tracking Number: 211732

TO: Ben Sackey
Location: REM 5B31
Art Unit : 1624
January 10, 2007

Case Serial Number: 10/762079

From: Kathleen Fuller
Location: EIC 1700
REMSEN 4B28
Phone: 571/272-2505
Kathleen.Fuller@uspto.gov

Search Notes

=> FILE REG
FILE 'REGISTRY' ENTERED AT 11:21:47 ON 10 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 JAN 2007 HIGHEST RN 917076-17-6
DICTIONARY FILE UPDATES: 9 JAN 2007 HIGHEST RN 917076-17-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 11:21:52 ON 10 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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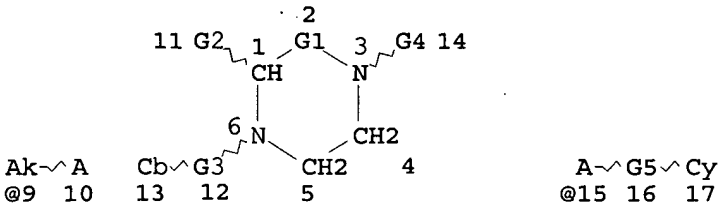
FILE COVERS 1907 - 10 Jan 2007 VOL 146 ISS 3
FILE LAST UPDATED: 9 Jan 2007 (20070109/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> D QUE L35
L19 STR

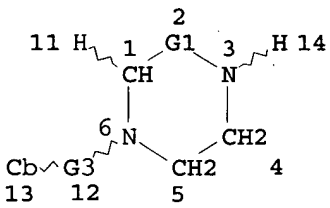


78,593 structures from query covering claim 1

VAR G1=CH2/7
VAR G2=H/9
REP G3=(3-5) A
VAR G4=H/A/15
REP G5=(0-5) A
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L21 SCR 146
L23 SCR 1211
L25 78593 SEA FILE=REGISTRY SSS FUL L19 AND L21 AND L23
L27 STR



Subset search to remove compounds where R_1 & R_2 are both hydrogen
3,753 – both H

VAR G1=CH2/7
REP G3=(3-5) A
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 12

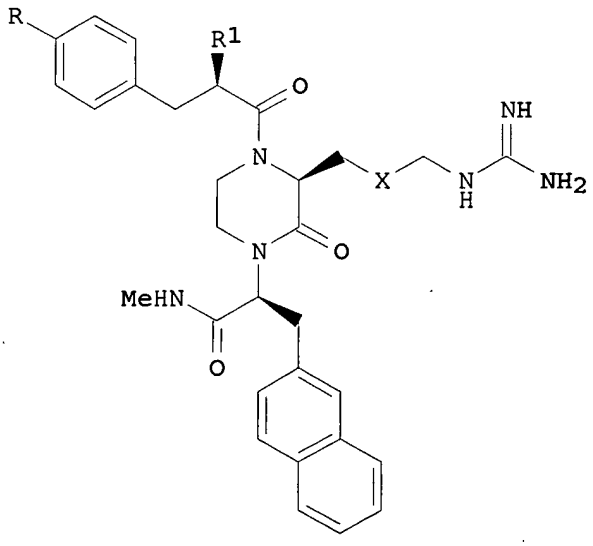
STEREO ATTRIBUTES: NONE
L30 3753 SEA FILE=REGISTRY SUB=L25 SSS FUL L27
L31 74840 SEA FILE=REGISTRY ABB=ON L25 NOT L30
L32 12685 SEA FILE=HCAPLUS ABB=ON L31
L33 39 SEA FILE=HCAPLUS ABB=ON L32 AND ?MELANOCORTIN?
L34 5930 SEA FILE=HCAPLUS ABB=ON L32(L)PREP/RL
L35 32 SEA FILE=HCAPLUS ABB=ON L33 AND L34

Too many hit RN's so only one per CA reference is printed

=> SEL HIT RN L35 1-32
E# OR SYSTEM LIMIT REACHED WHILE PROCESSING ANSWER 17
E1 THROUGH E999 ASSIGNED

=> D L35 BIB ABS IND FHITSTR 1-32

L35 ANSWER 1 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:757691 HCAPLUS
DN 145:357086
TI Design and synthesis of potent and selective 1,3,4-trisubstituted-2-oxopiperazine based **melanocortin**-4 receptor agonists
AU Tian, Xinrong; Mishra, Rajesh K.; Switzer, Adrian G.; Hu, X. Eric; Kim, Nick; Mazur, Adam W.; Ebetino, Frank H.; Wos, John A.; Crossdoersen, Doreen; Pinney, Beth B.; Farmer, Julie A.; Sheldon, Russell J.
CS Health Care Research Center, Procter & Gamble Pharmaceuticals, Mason, OH, 45040, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(17), 4668-4673
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 145:357086
GI



I

AB Peptidomimetics containing 1,3,4-trisubstituted-2-piperazinone moieties such

as I (R = H, F; R1 = H, H2N; X = bond, CH2) are prepared as human **melanocortin**-4 receptor (hMC4R) agonists. I (R = H, F; R1 = H, H2N; X = bond, CH2) bind to the hMC4R with Ki values of 5.3-11 nM and EC50 values of 1.7-9 nM; I (R = H, F; R1 = H, H2N; X = bond, CH2) have selectivities for hMC4R over the human **melanocortin**-1 receptor (hMC1R) of >50:1 and selectivities for hMC4R over the human **melanocortin**-3 receptor (hMC3R) of 10-50:1.

CC 34-3 (Amino Acids, Peptides, and Proteins)

ST piperazinone peptidomimetic prepn selective **melanocortin** receptor agonist; structure piperazinone contg peptidomimetic activity selectivity **melanocortin** receptor agonist

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 1; preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3; preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT Human
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT Structure-activity relationship
(receptor-binding; preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT **910567-93-0P 910567-94-1P 910568-03-5P**
910568-04-6P 910568-23-9P 910568-24-0P
910568-25-1P 910568-26-2P 910568-27-3P
910568-28-4P 910568-29-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT 459-31-4, 3-(4-Fluorophenyl)propanoic acid 142880-44-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT 910567-85-0P 910567-86-1P 910567-87-2P 910567-88-3P
910567-89-4P 910567-90-7P 910567-91-8P
910567-92-9P 910567-95-2P 910567-96-3P
910567-97-4P 910567-98-5P 910567-99-6P
910568-00-2P 910568-01-3P 910568-02-4P
910568-05-7P 910568-06-8P 910568-07-9P
910568-08-0P 910568-09-1P 910568-10-4P
910568-11-5P 910568-12-6P 910568-13-7P
910568-14-8P 910568-15-9P 910568-16-0P
910568-17-1P 910568-18-2P 910568-19-3P
910568-20-6P 910568-21-7P 910568-22-8P
910568-30-8P 910568-31-9P 910568-32-0P

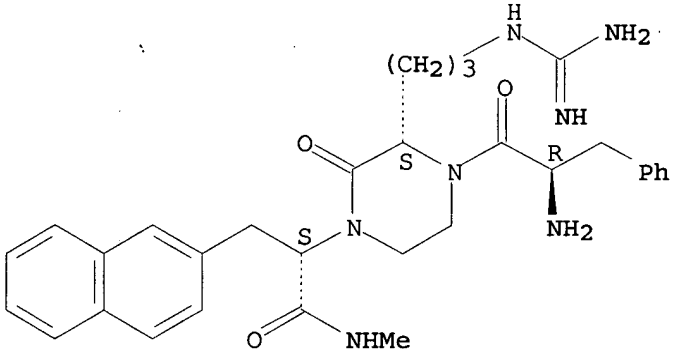
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT **910568-33-1P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

IT **910567-93-0P**
RL: PAC (Pharmacological activity); **PREP (Preparation)**; **PREP (Preparation)**; **PREP (Preparation)**
(preparation of nonracemic trisubstituted piperazinone-containing peptidomimetics, their activities as human MC4R agonists, and their selectivities for MC4R over MC1R and MC3R)

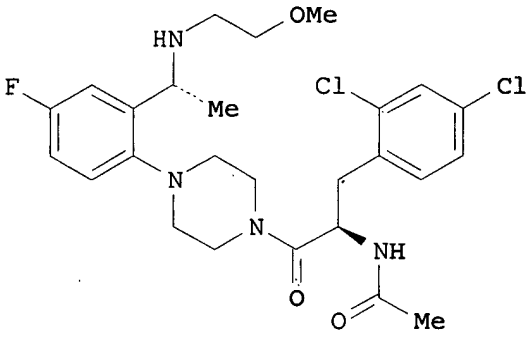
RN 910567-93-0 HCAPLUS
CN 1-Piperazineacetamide, 3-[3-[(aminoiminomethyl)amino]propyl]-4-[(2R)-2-amino-1-oxo-3-phenylpropyl]-N-methyl-α-(2-naphthalenylmethyl)-2-oxo-, (αS,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:665191 HCAPLUS
DN 145:336026
TI Synthesis of piperazinephen-1-ylethylamines as potent and selective antagonists of the human **melanocortin**-4 receptor
AU Tucci, Fabio C.; Tran, Joe A.; Jiang, Wanlong; Pontillo, Joseph; Marinkovic, Dragan; White, Nicole S.; Arellano, Melissa; Fleck, Beth A.; Wen, Jenny; Saunders, John; Foster, Alan C.; Chen, Chen
CS Department of Medicinal Chemistry, Neurocrine Biosciences, Inc., San Diego, CA, 92130, USA
SO Letters in Drug Design & Discovery (2006), 3(5), 311-315
CODEN: LDDDAW; ISSN: 1570-1808
PB Bentham Science Publishers Ltd.
DT Journal
LA English
GI



I

AB A series of piperazinephen-1-ylethylamines , e.g., I, were synthesized and evaluated for their biol. activity at the human **melanocortin**-4 receptor. This modification reduced the size and flexibility of the N-alkyl side-chain of some earlier lead compds., while maintained the low nanomolar binding affinity.

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST piperazinylphenylethylamine prepn human **melanocortin** receptor antagonist; chiral piperazinylphenylethylamine stereoselective prepn human **melanocortin** receptor antagonist; piperazine aryl deriv human **melanocortin** receptor antagonist

IT Amines, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(aliphatic, secondary, chiral; stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT Amines, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(amido, secondary; preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4, antagonists of; preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT Drug bioavailability
Human
Structure-activity relationship
(preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT Asymmetric synthesis and induction
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT Addition reaction
(stereoselective; stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT 909800-45-9P 909800-46-0P 909800-47-1P 909800-48-2P 909800-49-3P
909800-50-6P 909800-51-7P 909800-52-8P 909800-53-9P 909800-54-0P

909800-55-1P 909800-56-2P 909800-57-3P 909800-58-4P 909800-59-5P
909800-60-8P 909800-61-9P 909800-62-0P 909800-63-1P 909800-64-2P
909800-65-3P 909800-66-4P 909800-67-5P 909800-68-6P 909800-69-7P
909800-70-0P 909800-71-1P **909800-72-2P** 909800-73-3P
909800-74-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT 56-40-6, Glycine, reactions 56-41-7, L-Alanine, reactions 64-19-7, Acetic acid, reactions 67-62-9, Methoxyamine 75-04-7, Ethylamine, reactions 75-31-0, Isopropylamine, reactions 79-14-1, reactions 107-10-8, Propylamine, reactions 109-01-3 109-73-9, Butylamine, reactions 109-85-3 109-89-7, Diethylamine, reactions 110-76-9 110-85-0, Piperazine, reactions 110-91-8, Morpholine, reactions 123-75-1, Pyrrolidine, reactions 364-83-0 445-27-2 535-75-1, 2-Piperidinecarboxylic acid 541-41-3 598-74-3 1118-68-9 1759-53-1, Cyclopropanecarboxylic acid 1979-36-8 5332-73-0 18355-80-1 27035-32-1 30433-91-1, 2-Thiopheneethanamine 37143-54-7 57260-71-6 114873-12-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT 626219-18-9P 909799-93-5P 909799-95-7P 909799-97-9P 909799-99-1P
909800-01-7P 909800-03-9P 909800-05-1P 909800-07-3P 909800-09-5P
909800-11-9P 909800-13-1P 909800-15-3P 909800-17-5P 909800-19-7P
909800-21-1P 909800-23-3P 909800-25-5P 909800-27-7P 909800-29-9P
909800-30-2P 909800-31-3P 909800-32-4P 909800-33-5P 909800-35-7P
909800-37-9P 909800-38-0P 909800-39-1P 909800-40-4P
909800-43-7P 909800-44-8P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

IT 909800-84-6P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT 909800-79-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT 909800-82-4P 909800-83-5P 909800-85-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT 107-95-9, β-Alanine 2646-90-4 10312-83-1 196929-78-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human

melanocortin-4 receptor)

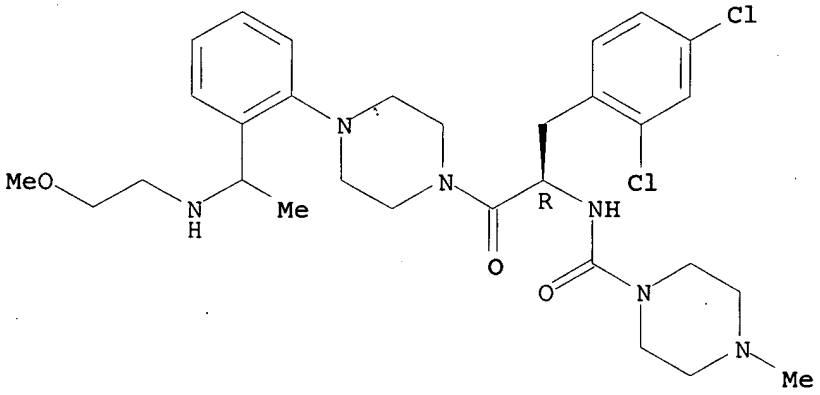
IT 697305-53-6P 869478-21-7P 869478-53-5P 909800-75-5P 909800-76-6P
909800-77-7P 909800-78-8P 909800-80-2P 909800-81-3P 909800-86-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective preparation and structure-activity relationship of chiral piperazinylphenylethylamines as antagonists of the human **melanocortin**-4 receptor)

IT **909800-72-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; **PREP (Preparation)**
(preparation and structure-activity relationship of piperazinylphenylethylamines as selective antagonists of the human **melanocortin**-4 receptor)

RN 909800-72-2 HCAPLUS

CN 1-Piperazinecarboxamide, N-[(1R)-1-[(2,4-dichlorophenyl)methyl]-2-[4-[2-[1-[(2-methoxyethyl)amino]ethyl]phenyl]-1-piperazinyl]-2-oxoethyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:499093 HCAPLUS
DN 145:159054
TI Privileged structure based ligands for **melanocortin**-4 receptors-Aliphatic piperazine derivatives
AU Briner, Karin; Collado, Ivan; Fisher, Matthew J.; Garcia-Paredes, Cristina; Husain, Saba; Kuklish, Steven L.; Mateo, Ana I.; O'Brien, Thomas P.; Ornstein, Paul L.; Zgombick, John; De Frutos, Oscar
CS Lilly Research Laboratories, Lilly Corporate Center, A Division of Eli Lilly and Company, Indianapolis, IN, 46258, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(13), 3449-3453
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 145:159054
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Analogs of the **melanocortin**-4 receptor binding (isoquinolinecarbonyl)chlorophenylalaninyl (diethylaminomethyl)benzylpiperazine I such as II are prepared The fluorophenyl group of I is replaced with aliphatic and alicyclic moieties to yield analogs; in addition, the tetrahydroisoquinolinecarbonyl moiety of I is replaced in some cases with a dihydroisoindolylacetyl group. Analogs replacing the fluorophenyl group of I with a cyclohexyl group show consistently high affinities for the human **melanocortin**-4 receptor. The diethylamino moiety of I can be replaced with polar groups with decreased basicities such as N-Et acetamides, N-ethylmethanesulfonamides, and succinimides. For example, II binds to the human **melanocortin**-4 receptor with a Ki value of 2 nM.

CC 1-3 (Pharmacology)
Section cross-reference(s): 28

ST aliph alicyclic substituted piperazine prepn **melanocortin4** receptor binding agent; structure piperazine human **melanocortin4** receptor binding activity

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT Human
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT Structure-activity relationship
(receptor-binding, **melanocortin**-4; preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT **444893-20-3P 444894-63-7P 444894-65-9P**
444894-68-2P 444894-92-2P 444895-43-6P
444895-47-0P 444895-51-6P 444895-61-8P
444895-63-0P 444895-67-4P 444898-25-3P
444898-26-4P 569654-52-0P **732979-35-0P**
733733-67-0P 785042-15-1P 791776-07-3P
900535-73-1P 900535-74-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT 85-41-6, Phthalimide 109-89-7, Diethylamine, reactions 110-91-8, Morpholine, reactions 120-92-3, Cyclopentanone 123-56-8, Succinimide 123-75-1, Pyrrolidine, reactions 405-50-5, 4-Fluorophenylacetic acid 590-86-3, 3-Methylbutanal 627-00-9, 4-Chlorobutanoic acid 701-97-3, Cyclohexanepropanoic acid 926-62-5, Isobutylmagnesium bromide 931-50-0, Cyclohexylmagnesium bromide 1123-00-8, Cyclopentaneacetic acid 2043-61-0, Cyclohexanecarboxaldehyde 4401-20-1, Cycloheptaneacetic acid 5292-21-7, Cyclohexaneacetic acid 5664-21-1, Cyclohexylacetaldehyde 35166-78-0, Cyclohexylmethylmagnesium bromide 42137-88-2, N,N-Bis(2-chloroethyl)-p-toluenesulfonamide 57260-71-6 252008-71-2 444583-56-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT 5445-17-0P, Methyl 2-bromopropanoate 37172-84-2P 58851-63-1P
71783-54-5P 191033-99-5P 191034-03-4P 444892-35-7P 444892-37-9P
444892-38-0P 444892-40-4P 444892-43-7P 444892-44-8P
444892-69-7P 444893-16-7P 444893-17-8P 444893-42-9P
444893-43-0P 444893-46-3P 444893-53-2P 444893-54-3P 444893-61-2P
444893-74-7P 444893-76-9P 444893-77-0P 444893-86-1P 444893-87-2P
444893-90-7P 444893-91-8P 444894-62-6P 444896-34-8P 444896-36-0P
444896-37-1P 444896-38-2P 444896-40-6P 444896-45-1P 569654-43-9P
569654-44-0P 569654-45-1P 569654-46-2P 900535-39-9P 900535-40-2P
900535-41-3P 900535-42-4P 900535-43-5P 900535-44-6P 900535-45-7P
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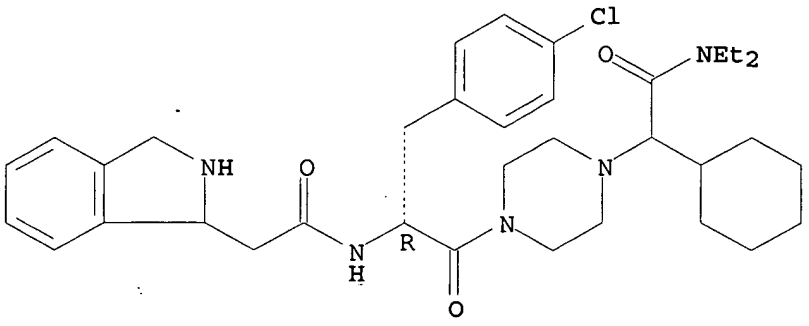
900535-51-5P 900535-52-6P 900535-53-7P **900535-54-8P**
900535-55-9P **900535-56-0P** **900535-57-1P**
900535-58-2P **900535-59-3P** 900535-60-6P
900535-61-7P **900535-62-8P** **900535-63-9P**
900535-64-0P **900535-65-1P** **900535-66-2P**
900535-67-3P **900535-68-4P** **900535-69-5P**
900535-70-8P **900535-71-9P** **900535-72-0P**
900535-75-3P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT 444896-39-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

IT **444893-20-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; **PREP (Preparation)**
(preparation of alkyl and cycloalkyl-substituted N-(tetrahydroisoquinolinylcarbonyl) and N-(dihydroisoindoleacetyl) p-chlorophenylalaninyl piperazines and their binding to the human **melanocortin**-4 receptor)

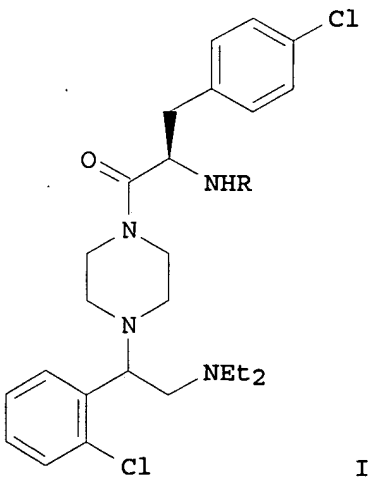
RN 444893-20-3 HCAPLUS
CN 1H-Isoindole-1-acetamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[1-cyclohexyl-2-(diethylamino)-2-oxoethyl]-1-piperazinyl]-2-oxoethyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

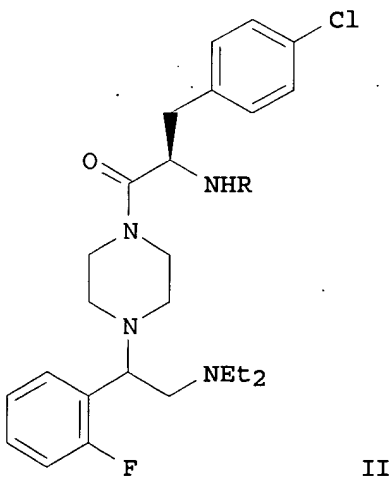


RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:274281 HCAPLUS
DN 144:468437
TI Synthesis and structure-activity relationships of novel dipeptides and reduced dipeptides as ligands for **melanocortin** subtype-4 receptor
AU Shi, Qing; Ornstein, Paul L.; Briner, Karin; Richardson, Timothy I.; Arnold, Macklin B.; Backer, Ryan T.; Buckmaster, Jennifer L.; Canada, Emily J.; Doecke, Christopher W.; Hertel, Larry W.; Honigschmidt, Nick; Hsiung, Hansen M.; Husain, Saba; Kuklish, Steve L.; Martinelli, Michael J.; Mullaney, Jeffrey T.; O'Brien, Thomas P.; Reinhard, Matt R.; Rothhaar, Roger; Shah, Jikesh; Wu, Zhipei; Xie, Chaoyu; Zgombick, John M.; Fisher, Matthew J.
CS Lilly Research Laboratories, Lilly Corporate Center, A Division of Eli Lilly and Company, Indianapolis, IN, 46285, USA
SO Bioorganic & Medicinal Chemistry Letters (2006), 16(9), 2341-2346
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
GI



I



II

AB A series of benzylic piperazines attached to a dipeptide core of H-D-Tic-D-p-Cl-Phe-OH has been identified as ligands for the **melanocortin** subtype-4 receptor (MC4R). Here, the authors describe the structure-activity relationship (SAR) studies on dipeptidyl D-p-chlorophenylalaninamides I [R = 2-(dihydroisoindol-1-yl)acetyl, 2-(tetrahydroisoquinolin-1-yl)acetyl] and II [R = 2-(dihydroisoindol-1-yl)acetyl, 2-(2-methyldihydroisoindol-1-yl)acetyl, 2-(tetrahydroisoquinolin-1-yl)acetyl, isoquinolin-3-ylcarbonyl, 1,1-dimethyltetrahydroisoquinolin-3-ylcarbonyl, tetrahydroisoquinolin-3-ylmethyl, etc.]. Several novel dipeptides and reduced dipeptides with high MC4R binding affinities and selectivity emerged from this SAR study.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST chlorophenylalaninamide dipeptide prepn ligand **melanocortin** receptor structure activity

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 1; preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3; preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 5; preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT Dipeptides
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT Structure-activity relationship
(receptor-binding, **melanocortin**; preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT **444896-32-6P 444897-00-1P 444897-48-7P**
444897-51-2P 444897-62-5P 444897-63-6P
444897-64-7P 444898-27-5P 444898-28-6P
886998-55-6P 886998-56-7P 886998-57-8P
886998-58-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT 444892-07-3P 444892-08-4P 886998-51-2P 886998-59-0P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin**

subtype-4 receptor)

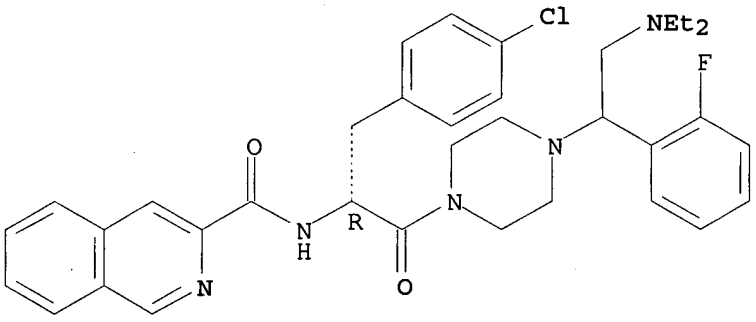
IT 96-33-3 775-06-4 5465-63-4 10544-63-5 57292-44-1 105400-81-5
115962-35-1 134166-72-6 444892-14-2 444895-01-6 444895-07-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT 34081-18-0P 162356-90-3P 171662-92-3P 444583-12-4P 444583-14-6P
444583-18-0P 444583-19-1P 444583-38-4P 444583-49-7P 444583-75-9P
444584-13-8P 444584-14-9P 444584-16-1P 444584-17-2P 444584-22-9P
444892-09-5P 444892-10-8P 444892-12-0P 444892-13-1P 444892-15-3P
444892-18-6P 444892-21-1P 444892-22-2P 444892-24-4P
444896-69-9P 444896-72-4P 760167-36-0P 886998-52-3P
886998-53-4P 886998-54-5P 886998-60-3P 886998-61-4P 886998-62-5P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

IT **444896-32-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; **PREP (Preparation)**
(preparation and structure-activity relationships of dipeptidyl chlorophenylalaninamides as ligands for **melanocortin** subtype-4 receptor)

RN 444896-32-6 HCAPLUS
CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-(diethylamino)-1-(2-fluorophenyl)ethyl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



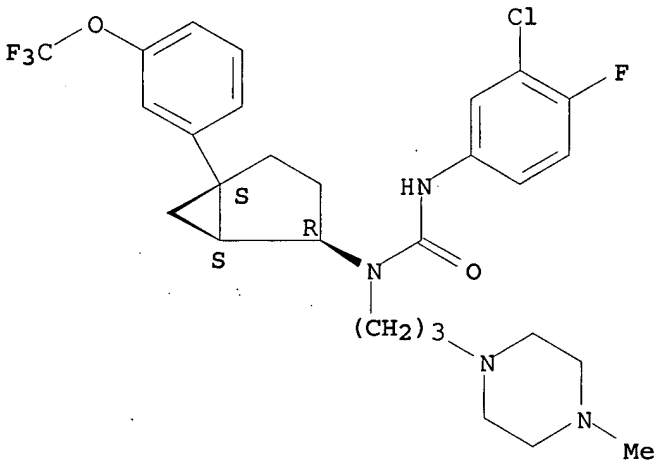
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:207048 HCAPLUS
DN 144:425101
TI Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents. Synthesis, SAR, and Biological Evaluation of Bicyclo[3.1.0]hexyl Ureas
AU McBriar, Mark D.; Guzik, Henry; Shapiro, Sherry; Paruchova, Jaroslava; Xu, Ruo; Palani, Anandan; Clader, John W.; Cox, Kathleen; Greenlee, William J.; Hawes, Brian E.; Kowalski, Timothy J.; O'Neill, Kim; Spar, Brian D.; Weig, Blair; Weston, Daniel J.; Farley, Constance; Cook, John
CS Department of Chemical Research and Department of Cardiovascular and Metabolic Diseases, Schering-Plough Research Institute, Kenilworth, NJ,

07033-0539, USA
SO Journal of Medicinal Chemistry (2006), 49(7), 2294-2310
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Melanin-concentrating hormone (MCH) is a cyclic, nonadecapeptide expressed in the
CNS of all vertebrates that regulates feeding behavior and energy homeostasis via interaction with the central **melanocortin** system. Regulation of this interaction results in modulation of food intake and body weight gain, demonstrating significant therapeutic potential for the treatment of obesity. The MCH-1 receptor (MCH-R1) has been identified as a key target in MCH regulation, as small mol. antagonists of MCH-R1 have demonstrated activity in vivo. Herein, we document our research in a bicyclo[3.1.0]hexyl urea series with particular emphasis on structure-activity relationships and optimization of receptor occupancy, measured both in vitro and via an ex vivo binding assay following an oral dosing regimen. Several compds. have been tested in vivo and exhibit oral efficacy in relevant acute rodent feeding models. In particular, 24u has proven efficacious in chronic rodent models of obesity, showing a statistically significant reduction in food intake and body weight over a 28 day
study.
CC 1-3 (Pharmacology)
Section cross-reference(s): 28
ST oral efficacy MCH R1 melanin concg hormone receptor antagonist; SAR prepn bicyclohexyl urea deriv
IT Drug bioavailability
Obesity
Structure-activity relationship
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT Melanin-concentrating hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MCH-1R (melanin-concentrating hormone receptor 1); Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT Drug delivery systems
(oral; Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT 67382-96-1, Melanin-concentrating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT 540783-32-2P 540783-33-3P 540783-37-7P **540783-45-7P**
540783-49-1P 540783-64-0P **540783-65-1P** 540783-66-2P
540783-74-2P **540783-78-6P** **540783-79-7P**
540783-93-5P **885323-06-8P** **885323-08-0P**
885323-09-1P **885323-10-4P** **885323-30-8P**
885323-31-9P **885323-32-0P** **885323-33-1P**
885323-34-2P **885323-35-3P** **885323-36-4P**
885323-37-5P **885323-38-6P** **885323-39-7P**
885323-40-0P **885323-41-1P** **885323-42-2P**
885323-43-3P **885323-44-4P** 885323-45-5P 885323-47-7P
885323-48-8P 885323-49-9P 885323-50-2P 885323-51-3P 885323-52-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**;
USES (Uses)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1

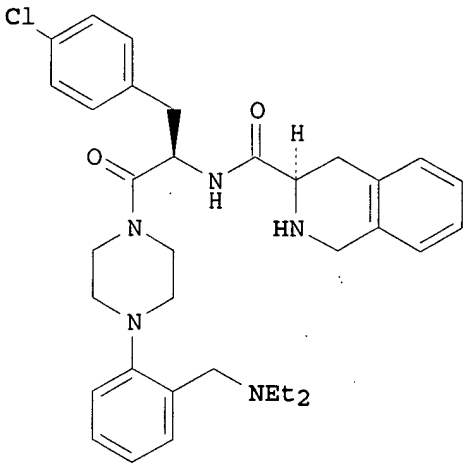
Antagonists as Antiobesity Agents)
IT 443997-61-3 515141-51-2 540783-35-5 638191-35-2 848779-65-7
862556-72-7 870766-17-9 885322-92-9 885323-46-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT 50-00-0, Formaldehyde, reactions 75-11-6 75-36-5, Acetyl chloride
98-80-6 108-36-1 109-01-3 110-89-4, Piperidine, reactions
110-91-8, Morpholine, reactions 124-63-0, Methanesulphonyl chloride
590-86-3 768-35-4 934-98-5 1692-25-7 1765-93-1 4248-19-5,
tert-Butyl carbamate 4489-53-6 4572-03-6, 1-(3-Aminopropyl)-4-methylpiperazine 4683-50-5 5720-07-0 6165-69-1 6952-59-6
7154-73-6, 1-(2-Aminoethyl)pyrrolidine 10365-98-7 13325-10-5,
4-Aminobutanol 17933-03-8 24424-99-5 30418-59-8 34893-92-0
50529-33-4 51865-32-8 63503-60-6 116370-63-9 **117009-98-0**
126747-14-6 139057-86-6 139301-27-2 149104-88-1 156545-07-2
168267-41-2 179113-90-7 214210-21-6 373384-18-0 843663-18-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT 109526-42-3P 540783-30-0P **540787-83-5P** 540787-85-7P
849697-75-2P 849697-79-6P 849697-80-9P 849697-82-1P 849697-83-2P
885322-93-0P 885322-95-2P **885322-96-3P 885322-97-4P**
885322-98-5P 885322-99-6P 885323-01-3P 885323-02-4P
885323-03-5P **885323-04-6P 885323-05-7P** 885323-07-9P
885323-11-5P 885323-12-6P 885323-13-7P 885323-14-8P 885323-15-9P
885323-16-0P 885323-17-1P 885323-18-2P 885323-19-3P 885323-20-6P
885323-21-7P 885323-22-8P 885323-23-9P 885323-24-0P 885323-25-1P
885323-26-2P 885323-27-3P 885323-28-4P 885323-29-5P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
IT **540783-45-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(Discovery of Orally Efficacious Melanin-Concentrating Hormone Receptor-1 Antagonists as Antiobesity Agents)
RN 540783-45-7 HCAPLUS
CN Urea, N'-(3-chloro-4-fluorophenyl)-N-[3-(4-methyl-1-piperazinyl)propyl]-N-[(1R,2S,5R)-5-[3-(trifluoromethoxy)phenyl]bicyclo[3.1.0]hex-2-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1084918 HCAPLUS
DN 144:36494
TI Privileged structure based ligands for **melanocortin** receptors - Substituted benzylic piperazine derivatives
AU Fisher, Matthew J.; Backer, Ryan T.; Collado, Ivan; De Frutos, Oscar; Husain, Saba; Hsiung, Hansen M.; Kuklish, Steve L.; Mateo, Ana I.; Mullaney, Jeffrey T.; Ornstein, Paul L.; Paredes, Cristina Garcia; O'Brian, Thomas P.; Richardson, Timothy I.; Shah, Jikesh; Zgombick, John M.; Briner, Karin
CS Lilly Research Laboratories, Lilly Corporate Center, A Division of Eli Lilly and Company, Indianapolis, IN, 46258, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(22), 4973-4978
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
GI



I

AB Replacement of the arylpiperazine moiety in I with a variety of substituted benzylic piperazines yields compds. that afford **melanocortin** receptor 4 (MCR4) activity. Analogs with ortho substitution on the aromatic ring afforded the highest affinity. Resolution of the stereocenter of the benzylic piperazine based privileged structure revealed that the R-enantiomer was more active.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST benzylpiperazinamide isoquinolinecarbonylphenylalanine prepn **melanocortin** receptor 4 affinity

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of isoquinolinecarbonylphenylalanine benzylpiperazinamides with **melanocortin** receptor 4 activity)

IT 444580-18-1DP, analogs **444892-89-1P 444897-33-0P**
444897-46-5P 444897-47-6P 444897-54-5P
444897-55-6P 444897-57-8P 444897-65-8P
444897-78-3P 444897-81-8P 444897-95-4P
444897-99-8P 444898-08-2P 444898-13-9P
444898-14-0P 444898-15-1P 444898-16-2P
741244-49-5P 764641-75-0P 870701-33-0P
870701-34-1P 870701-35-2P 870701-36-3P
870701-37-4P 870701-38-5P 870701-39-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of isoquinolinecarbonylphenylalanine benzylpiperazinamides with **melanocortin** receptor 4 activity)

IT 85-44-9, Phthalic anhydride 103-82-2, Phenylacetic acid, reactions 501-52-0, 3-Phenylpropanoic acid 584-74-7, Ethyl 2-fluorobenzeneacetate 1821-12-1, 4-Phenylbutyric acid 2270-20-4, 5-Phenylpentanoic acid 2759-28-6, N-Benzylpiperazine 20989-17-7, (S)-Phenylglycinol 57260-71-6, N-tert.-Butoxycarbonylpiperazine 69628-75-7, 1-(1-Phenylethyl)piperazine 252008-71-2 444892-55-1 444894-06-8 444894-12-6 444894-13-7 444894-15-9 444894-41-1 444894-42-2 444894-46-6 870701-28-3 870701-29-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoquinolinecarbonylphenylalanine benzylpiperazinamides with **melanocortin** receptor 4 activity)

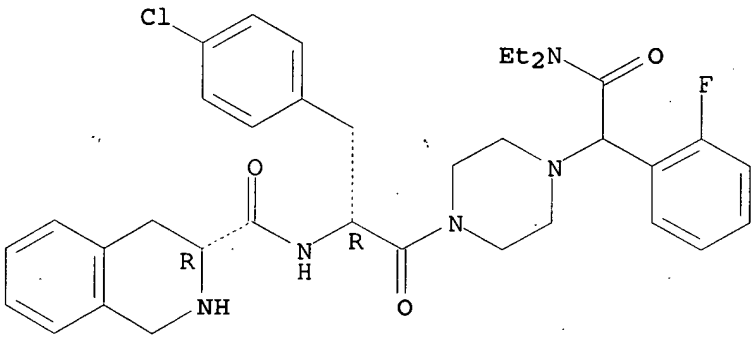
IT 135357-91-4P 444892-81-3P 444893-22-5P 444893-30-5P 444894-08-0P
444894-10-4P 444894-11-5P 444894-21-7P 444894-31-9P 444894-34-2P
444895-34-5P 870701-30-7P 870701-31-8P 870701-32-9P 870701-40-9P
870701-41-0P 870701-42-1P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of isoquinolinecarbonylphenylalanine benzylpiperazinamides with **melanocortin** receptor 4 activity)

IT **444892-89-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; **PREP (Preparation)**
(preparation of isoquinolinecarbonylphenylalanine benzylpiperazinamides with **melanocortin** receptor 4 activity)

RN 444892-89-1 HCAPLUS

CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-(diethylamino)-1-(2-fluorophenyl)-2-oxoethyl]-1-piperazinyl]-2-oxoethyl]-1,2,3,4-tetrahydro-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:527392 HCAPLUS
DN 143:20084
TI Naphthalene-containing **melanocortin** receptor-specific small molecule
IN Sharma, Shubh D.; Shadiack, Annette M.; Shi, Yi-Qun; Wu, Zhijun; Rajpurohit, Ramesh; Burris, Kevin; Purma, Papireddy
PA Palatin Technologies, Inc., USA
SO U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 837,519.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 11

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005130988	A1	20050616	US 2005-36282	20050114
WO 2003013571	A1	20030220	WO 2002-US25574	20020812

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

applicants

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004152134 A1 20040805 US 2004-761889 20040121
US 2004157264 A1 20040812 US 2004-762079 20040121
WO 2005102340 A1 20051103 WO 2004-US1462 20040121
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004224957 A1 20041111 US 2004-837519 20040430
PRAI US 2001-311404P P 20010810
WO 2002-US25574 A2 20020812
US 2003-467442P P 20030501
US 2003-474497P P 20030530
US 2004-536606P P 20040114
US 2004-761889 A2 20040121
US 2004-762079 A2 20040121
US 2004-546393P P 20040219
US 2004-559741P P 20040405
US 2004-563739P P 20040419
US 2004-837519 A2 20040430
OS MARPAT 143:20084
AB A method of modulating energy homeostasis in a mammal without eliciting a sexual response by administration of a therapeutically effective amount of a pharmaceutical composition including a **melanocortin** receptor compound of the formula I (where R1 = a bond or a linker unit including from one to six backbone atoms and an unsubstituted naphthalene group, L = a conformationally restricted ring system consisting of a single ring or bicyclic nonarom. carbocyclic ring system, etc., R2= -(CH2)4NH2,-(CH2)3NHC(NH2)=NH, etc., R3 = L-or D-isomer of Phe, Phe(4-F), Phe(4-Br), etc., and Rx = H, C-C6 aliphatic linear chain, etc.).
IC ICM A61K031-495
ICS A61K031-496
INCL 514253110; 514254050; 514255030; 514249000
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 25, 27
ST naphthalene **melanocortin** receptor mol energy homeostasis
IT Drug delivery systems
(injections, i.c.v; naphthalene-containing **melanocortin** receptor-specific small mol.)
IT Drug delivery systems
(injections, i.v.; naphthalene-containing **melanocortin** receptor-specific small mol.)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 1; naphthalene-containing **melanocortin** receptor-specific small mol.)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3; naphthalene-containing **melanocortin** receptor-specific small mol.)
IT Pituitary hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; naphthalene-containing **melanocortin** receptor-specific small mol.)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 5; naphthalene-containing **melanocortin** receptor-specific small mol.)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; naphthalene-containing **melanocortin** receptor-specific small mol.)

IT Appetite
Homeostasis
Melanoma
(naphthalene-containing **melanocortin** receptor-specific small mol.)

IT Sexual behavior
(penile erection; naphthalene-containing **melanocortin** receptor-specific small mol.)

IT 91-20-3, Naphthalene, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(naphthalene-containing **melanocortin** receptor-specific small mol.)

IT **497934-95-9P 497935-00-9P 497935-06-5P**
497935-81-6P 497935-84-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(naphthalene-containing **melanocortin** receptor-specific small mol.)

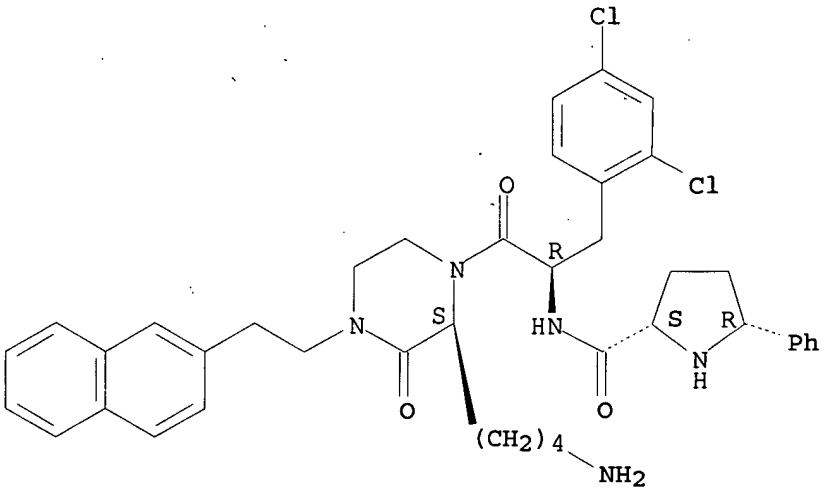
IT **738600-26-5P** 791624-89-0P 791624-91-4P 791624-95-8P
791624-96-9P 791624-97-0P 791625-01-9P 791625-03-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(naphthalene-containing **melanocortin** receptor-specific small mol.)

IT 581-96-4, 2-Naphthylacetic acid 2799-16-8, (R)-(-)-1-Amino-2-propano
2799-17-9, (S)-(+)-1-Amino-2-propanol 21705-13-5, D-Alanine methyl e
35320-23-1, (R)-(-)-2-Amino-1-propanol 57292-44-1 114873-12-0
143824-77-5 791625-57-5 791625-59-7 853029-92-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(naphthalene-containing **melanocortin** receptor-specific small mol.)

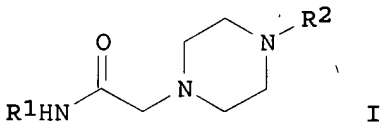
IT **497934-95-9P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; USES (Uses)
(naphthalene-containing **melanocortin** receptor-specific small mol.)

RN 497934-95-9 HCAPLUS
CN 2-Pyrrolidinecarboxamide, N-[(1R)-2-[(2S)-2-(4-aminobutyl)-4-[2-(2-naphthalenyl)ethyl]-3-oxo-1-piperazinyl]-1-[(2,4-dichlorophenyl)methyl]-2-oxoethyl]-5-phenyl-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L35 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:430643 HCAPLUS
DN 144:212739
TI Application of a photolabile backbone amide linker for cleavage of internal amides in the synthesis towards **melanocortin** subtype-4 agonists
AU Minkwitz, Rolf; Meldal, Morten
CS Carlsberg Laboratory, SPOCC Centre, Valby, DK-2500, Den.
SO QSAR & Combinatorial Science (2005), 24(3), 343-353
CODEN: QCSSAU; ISSN: 1611-020X
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal
LA English
OS CASREACT 144:212739
GI



I

AB A new photolabile backbone amide handle has been developed for the synthesis of a **melanocortin** subtype-4 receptor (MCR4) agonist library on the solid phase. This traceless linker allows for the solid-supported synthesis of internal amides and their release under very mild, orthogonal conditions from solid support. The chemical to attach an amide onto the linker is discussed. Structural variations of the linker in order to facilitate the attachment are investigated. The cleavage rate on the solid phase was measured. Finally, a small (piperazinyl)acetamide I [R1 = PhCH2CH2, (R)-PhCHMe, 2-(3-indolyl)ethyl; R2 = PhCH2CH2, 3-pyridylmethyl, 2-(3-indolyl)ethyl, 1,2,4-oxadiazol-3-ylmethyl] library was synthesized using this photolabile linker.
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
ST acetamide piperazinyl solid phase synthesis; photolabile amide backbone linker prepn cleavage

IT Photolysis
(photochem. bond cleavage; solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT Bond cleavage
(photochem.; solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT Linking agents
Solid phase synthesis
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT Amides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

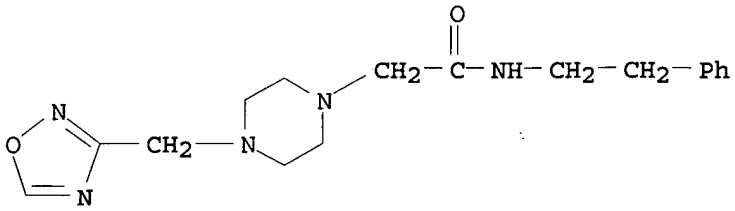
IT 61-54-1, Tryptamine 64-04-0, 2-Phenylethylamine 103-63-9, 2-Phenylethyl bromide 110-85-0, Piperazine, reactions 121-33-5, Vanillin 501-52-0, 3-Phenylpropionic acid 2969-81-5, Ethyl 4-bromobutyrate 3006-96-0, 4-(Hydroxymethyl)benzoic acid 3389-21-7, 3-(2-Bromoethyl)indole 3886-69-9, (R)-α-Methylbenzylamine 4897-84-1, Methyl 4-bromobutyrate 5150-42-5, 2,3-Dimethoxyphenol 6959-48-4, 3-(Chloromethyl)pyridine hydrochloride 51791-12-9, 3-(Chloromethyl)-1,2,4-oxadiazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT 19283-70-6P 69471-05-2P 176375-41-0P 176375-42-1P 263758-69-6P 875766-92-0P 875766-93-1P 875766-94-2P 875766-95-3P 875766-96-4P 875766-97-5P 875766-98-6DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875766-99-7DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875767-00-3DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875767-04-7DP, phenylpropionic acid-modified poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT 13156-95-1P 36293-00-2P 52191-26-1P 875767-01-4DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875767-02-5DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875767-03-6DP, poly(ethylene glycol)-poly(dimethylacrylamide) resin-supported 875767-05-8P 875767-06-9P 875767-07-0P 875767-08-1P **875767-09-2P 875767-10-5P 875767-11-6P 875767-12-7P 875767-13-8P 875767-14-9P 875767-15-0P 875767-16-1P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and photochem. cleavage of internal amides)

IT **875767-09-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(solid-phase synthesis of (piperazinyl)acetamides using PEGA-resin supported photolabile backbone amide linker via formation and

photochem. cleavage of internal amides)
RN 875767-09-2 HCAPLUS
CN 1-Piperazineacetamide, 4-(1,2,4-oxadiazol-3-ylmethyl)-N-(2-phenylethyl)-(9CI) (CA INDEX NAME)

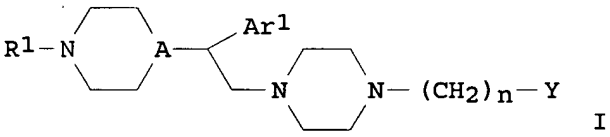


RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:120093 HCAPLUS
DN 142:191300
TI Use of piperazine derivatives as MC4 receptor antagonists and therapeutic agents containing them for treatment anxiety neurosis or depression
IN Nakazato, Atsuro; Ishii, Takaaki; Nozawa, Hiroshi
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 52 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005035983	A	20050210	JP 2004-179381	20040617
PRAI JP 2003-181040	A	20030625		

OS MARPAT 142:191300
GI



I

AB Piperazine derivs I [n = 1-8; R1 = H, C1-10 alkyl; A = CH, N; Ar1 = Ph substituted with 1-3 groups selected from , C1-10 alkyl, C1-10 alkoxy, aralkyloxy, OH, halo, NO2, amino, mono- or di-C1-6 alkyl-amino, CF3, OCF3, cyano, carbamoyl, and Ph; Y = Y1Y2Ar2; Y1Y2 = direct bond, O, CO, CH:CH, CONR2, NR2CO (R2 = H, C1-10 alkyl); Ar2 = phthalimide-1-yl, dibenzofuranyl, C3-10 cycloalkyl, C2-9 oxacycloalkyl, C2-9 lactam-1-yl, 1H-quinazoline-1,4-dion-1-yl, etc.] or their pharmaceutically acceptable salts are useful as MC4R (**melanocortin** receptor type 4) antagonists. Anxiolytics or antidepressants containing I or their salts are also claimed. Thus, IC50 I (n = 3, R1 = CHMe2, A = N, Ar1 = C6H4F-4, Y = 2,4-diphenyl-5-thiazolyl) against human MC4R expressed in HEK 293 was 162 nM.
IC ICM C07D209-48

ICS A61K031-427; A61K031-496; A61K031-506; A61P005-04; A61P025-22; A61P025-24; A61P043-00; C07D211-18; C07D211-32; C07D225-02; C07D231-12; C07D231-20; C07D239-26; C07D239-42; C07D239-96; C07D261-08; C07D263-32; C07D277-20; C07D277-28

CC 1-11 (Pharmacology)
Section cross-reference(s): 28

ST piperazine deriv prepn **melanocortin** receptor type 4 antagonist; MC4R antagonist pipearazinoethylpiperazine anxiety neurosis depression treatment

IT Mental and behavioral disorders
(depression; preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT Mental and behavioral disorders
(neurosis; preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT Antidepressants
Anxiety
Anxiolytics
Human
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT **552885-56-0P 552885-58-2P 552885-59-3P**
552885-61-7P 552885-62-8P 552885-63-9P 552885-66-2P 552885-67-3P
552885-69-5P 552885-70-8P **552885-73-1P 552885-76-4P**
552885-85-5P, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]-4-(4-cyclooctyl-4-oxobutyl)piperazine **552885-87-7P**
552885-90-2P 707542-35-6P 756473-47-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT **552884-23-8P 552884-24-9P 552884-25-0P**
552884-26-1P 552884-27-2P 552884-28-3P
552884-29-4P 552884-30-7P 552884-31-8P
552884-32-9P 552884-33-0P 552884-34-1P
552884-35-2P 552884-36-3P 552884-37-4P
552884-38-5P 552884-39-6P 552884-40-9P
552884-41-0P 552884-42-1P 552884-43-2P
552884-44-3P 552884-45-4P 552884-46-5P
552884-47-6P 552884-48-7P 552884-49-8P
552884-50-1P 552884-51-2P 552884-52-3P
552884-53-4P 552884-54-5P 552884-55-6P
552884-56-7P 552884-57-8P 552884-58-9P
552884-59-0P **552884-60-3P 552884-61-4P**
552884-62-5P 552884-63-6P 552884-64-7P
552884-65-8P 552884-66-9P 552884-67-0P
552884-68-1P 552884-69-2P 552884-70-5P
552884-71-6P 552884-72-7P 552884-73-8P
552884-74-9P 552884-75-0P 552884-76-1P
552884-77-2P 552884-79-4P 552884-80-7P 552884-81-8P
552884-82-9P 552884-84-1P 552884-85-2P
552884-86-3P 552884-89-6P 552884-90-9P

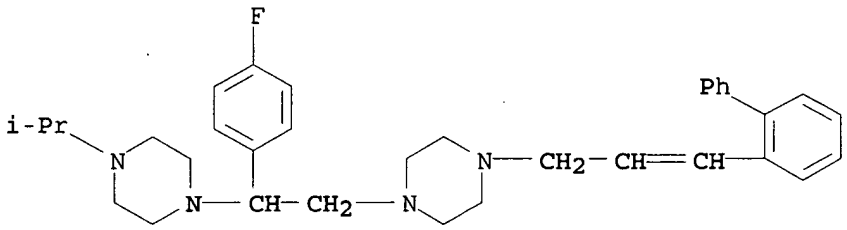
552884-91-0P 552884-92-1P 552884-93-2P
552884-94-3P 552884-95-4P 552884-97-6P
552884-98-7P 552884-99-8P 552885-01-5P
552885-02-6P 552885-03-7P 552885-04-8P
552885-06-0P 552885-07-1P 552885-08-2P 552885-09-3P
552885-10-6P 552885-11-7P 552885-12-8P 552885-13-9P 552885-14-0P
552885-15-1P 552885-16-2P 552885-17-3P 552885-19-5P 552885-20-8P
552885-21-9P 552885-22-0P 552885-24-2P 552885-26-4P 552885-28-6P
552885-30-0P 552885-32-2P **552885-34-4P**
552885-36-6P 552885-39-9P 552885-43-5P
552885-44-6P 552885-46-8P 552885-47-9P 552885-48-0P
552885-49-1P 552885-50-4P 552885-51-5P **838819-87-7P**
838819-88-8P 838819-90-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT 50-01-1, Guanidine hydrochloride 120-43-4, 1-Ethoxycarbonylpiperazine 405-50-5, p-Fluorophenylacetic acid 456-04-2, 2-Chloro-4'-fluoroacetophenone 19853-17-9, [1,1'-Biphenyl]-2-propanoic acid 31166-44-6, 1-Benzyloxycarbonylpiperazine 79099-07-3, 1-tert-Butoxycarbonyl-4-piperidone 88569-66-8, 1-Isopropylpiperazine dihydrochloride 552885-57-1 552885-60-6 **552885-64-0**
552885-71-9 552885-75-3, 2-Acetyl-4'-fluorobiphenyl
552885-84-4, 4-Bromo-1-cyclooctylbutan-1-one **552885-88-8**
552885-91-3 838819-91-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT 89011-47-2P, 1-Ethoxycarbonyl-4-[2-(4-fluorophenyl)-2-hydroxyethyl]piperazine hydrochloride 106000-09-3P, 1-Ethoxycarbonyl-4-[2-chloro-2-(4-fluorophenyl)ethyl]piperazine 385844-14-4P
385844-15-5P, 1-tert-Butoxycarbonyl-4-[carboxy-(4-fluorophenyl)methyl]-3,6-dihydro-2H-pyridine 552885-52-6P **552885-53-7P**
552885-65-1P 552885-68-4P 552885-72-0P
552885-74-2P 552885-77-5P, 1-tert-Butoxycarbonyl-4-[carboxy-(4-fluorophenyl)methyl]piperidine **552885-78-6P**,
1-Benzyloxycarbonyl-4-[2-(1-tert-butoxycarbonylpiperidin-4-yl)-2-(4-fluorophenyl)acetyl]piperazine **552885-79-7P**,
1-Benzyloxycarbonyl-4-[2-(4-fluorophenyl)-2-(1-isopropylpiperidin-4-yl)acetylpiperazine 552885-80-0P, 2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)-1-piperazin-1-ylethanone 552885-83-3P,
1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]piperazine
552885-86-6P, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]piperazine trihydrochloride 686710-22-5P **838819-92-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

IT **552885-56-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of (piperazinyl or piperidinyl)ethylpiperazine derivs. as MC4 receptor antagonists for treatment of anxiety neurosis and depression)

RN 552885-56-0 HCAPLUS
CN Piperazine, 1-(3-[1,1'-biphenyl]-2-yl-2-propenyl)-4-[2-(4-fluorophenyl)-2-[4-(1-methylethyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L35 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:652533 HCAPLUS
DN 141:191073
TI Preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists.
IN Sharma, Shubh D.; Shi, Yi-qun; Wu, Zhijun; Rajpurohit, Ramesh
PA Palatin Technologies, Inc., USA
SO U.S. Pat. Appl. Publ., 70 pp., Cont.-in-part of Appl. No. PCT/US02/25574.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 11

applicants

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004157264	A1	20040812	US 2004-762079	20040121
	WO 2003013571	A1	20030220	WO 2002-US25574	20020812
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2005102340	A1	20051103	WO 2004-US1462	20040121
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005130988	A1	20050616	US 2005-36282	20050114
	US 2005124636	A1	20050609	US 2005-40838	20050121
	US 2005176728	A1	20050811	US 2005-99814	20050405
PRAI	US 2001-311404P	P	20010810		
	WO 2002-US25574	A2	20020812		
	US 2003-474497P	P	20030530		
	US 2003-467442P	P	20030501		
	US 2004-536606P	P	20040114		
	US 2004-538100P	P	20040121		
	US 2004-761889	A2	20040121		
	US 2004-762079	A2	20040121		

US 2004-546393P P 20040219
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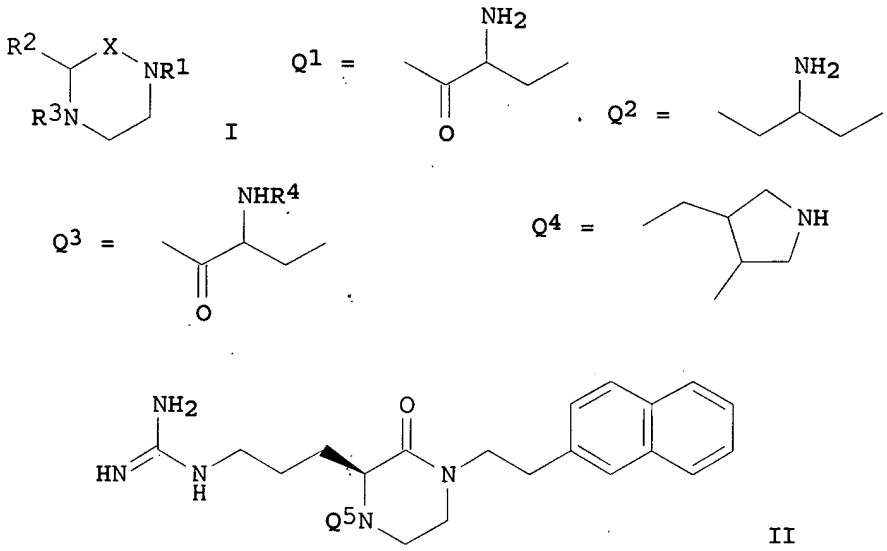
US 2004-563739P P 20040419
US 2004-837519 A2 20040430
OS MARPAT 141:191073
GI



AB Title compds. [I; R1 = L1J, H; R2 = (CH2)yW, J, L1J; R3 = L2Q; L1 = (CH2)y, O(CH2)y, NH(CH2)y, CO(CH2)y, CO2(CH2)y, CH2CONH; J = (substituted) aryl, carbocyclyl, carbobicyclyl, heterobicyclyl; W = heteroatom unit with ≥1 cationic center, hydrogen bond donor, or hydrogen bond acceptor wherein ≥1 atom = N; L2 = Q1, Q2, Q3, Q4, etc.; Q = (substituted) Ph, naphthyl; R4 = H, R5, R5R6; R5 = amino acid residue, amine capping group; R6 = H, amine capping group; y = 1-6], were prepared Thus, title compound (II; Q5 = 2,4-dichloro-D-phenylalanyl) (general preparation given) at 1 μM gave 95% inhibition of **melanocortin** MC4-R.

IC ICM G01N033-53
ICS C07D043-02
INCL 435007100; 544372000; 544386000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
ST piperazine prepn **melanocortin** receptor agonist antagonist; peptidylpiperazine prepn sexual dysfunction eating disorder cachexia treatment
IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(derivs.; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)
IT Homeostasis
(energy homeostasis impairment treatment; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)
IT Pituitary hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 1; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 5; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Antiobesity agents
Human
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT Cachexia
Eating disorders
Obesity
Sexual disorders
(treatment; preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT **497934-80-2P 497934-81-3P 497934-84-6P**
497934-85-7P 497934-86-8P 497934-88-0P
497934-89-1P 497934-90-4P 497934-91-5P
497934-93-7P 497934-94-8P 497934-95-9P
497934-96-0P 497934-97-1P 497934-98-2P
497935-01-0P 497935-04-3P 497935-05-4P
497935-06-5P 497935-07-6P 497935-08-7P
497935-09-8P 497935-10-1P 497935-11-2P
497935-12-3P 497935-13-4P 497935-14-5P
497935-15-6P 497935-16-7P 497935-17-8P
497935-18-9P 497935-19-0P 497935-20-3P
497935-21-4P 497935-22-5P 497935-23-6P
497935-24-7P 497935-25-8P 497935-26-9P
497935-27-0P 497935-28-1P 497935-29-2P
497935-30-5P 497935-31-6P 497935-32-7P
497935-33-8P 497935-34-9P 497935-35-0P
497935-36-1P 497935-37-2P 497935-38-3P
497935-39-4P 497935-40-7P 497935-41-8P
497935-42-9P 497935-43-0P 497935-44-1P
497935-45-2P 497935-46-3P 497935-47-4P

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738600-03-8P 738600-04-9P 738600-05-0P
738600-06-1P 738600-07-2P 738600-08-3P
738600-09-4P 738600-10-7P 738600-11-8P
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738600-18-5P 738600-19-6P 738600-20-9P
738600-21-0P 738600-22-1P 738600-23-2P
738600-24-3P 738600-25-4P 738600-26-5P
738600-27-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT **738600-28-7 738600-29-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

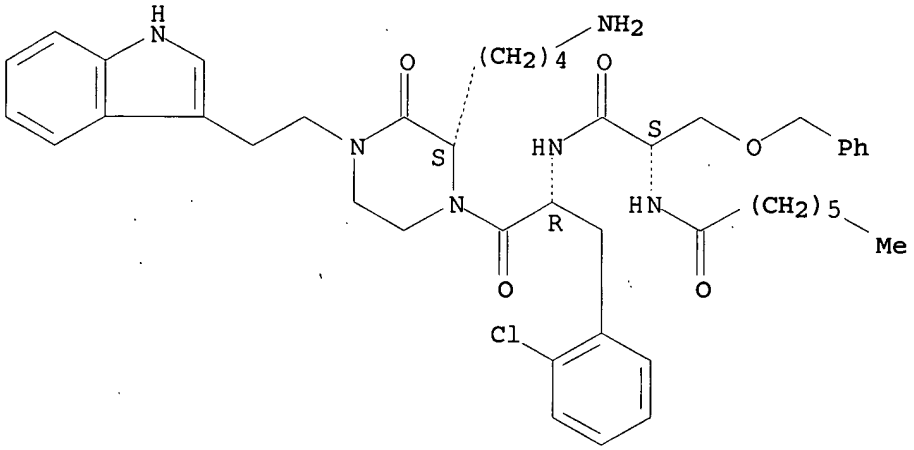
IT 104-63-2 2640-58-6 22509-74-6, N-Carboethoxyphthalimide 70080-13-6, 2-Naphthylacetaldehyde 107819-90-9 109425-55-0 114873-12-0 245488-90-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

IT 7767-00-2P 497934-78-8P 497934-79-9P 497936-48-8P 497936-49-9P 497936-50-2P **497936-51-3P 497936-52-4P**
497936-53-5P 738600-30-1P 738600-31-2P
738600-32-3P 738600-33-4P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

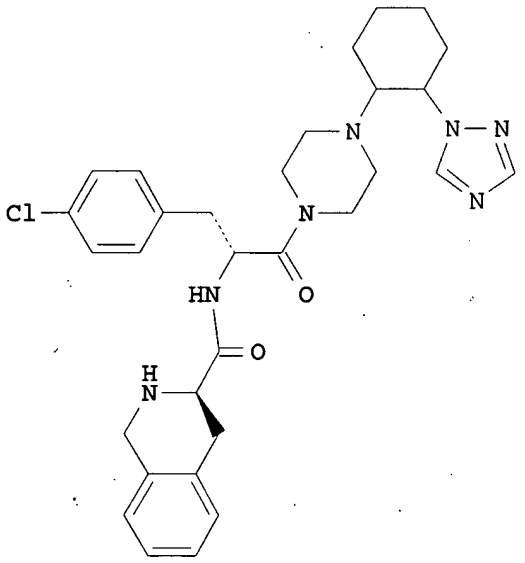
IT **497934-80-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazines as **melanocortin**-specific agonists, antagonists, or mixed agonists and antagonists)

RN 497934-80-2 HCAPLUS
CN Heptanamide, N-[(1S)-2-[[(1R)-2-[(2S)-2-(4-aminobutyl)-4-[2-(1H-indol-3-yl)ethyl]-3-oxo-1-piperazinyl]-1-[(2-chlorophenyl)methyl]-2-oxoethyl]amino]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L35 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:617800 HCAPLUS
DN 141:314297
TI New Substituted Piperazines as Ligands for **Melanocortin** Receptors. Correlation to the X-ray Structure of "THIQ"
AU Mutulis, Felikss; Yahorava, Sviatlana; Mutule, Ilze; Yahorau, Aleh; Liepinsh, Edvards; Kopantshuk, Sergei; Veiksina, Santa; Tars, Kaspars; Belyakov, Sergey; Mishnev, Anatoly; Rinken, Ago; Wikberg, Jarl E. S.
CS Department of Pharmaceutical Biosciences, Division of Pharmacology, Uppsala University, Uppsala, SE-751 24, Swed.
SO Journal of Medicinal Chemistry (2004), 47(18), 4613-4626
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:314297
GI



I

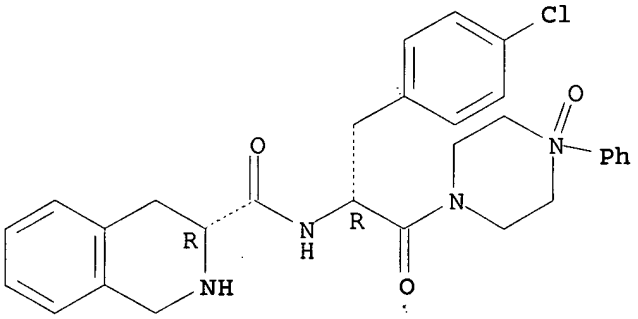
AB A series of piperazine analogs of the **melanocortin** 4 receptor (MC4R) specific small-mol. agonist THIQ was synthesized and characterized structurally and pharmacol. First, several THIQ imitations lacking the triazole moiety were prepared Syntheses included acylation of 4-phenylpiperazine or 4-cyclohexylpiperazine. In two cases the tertiary amine function was replaced by the N-oxide. To obtain more complex structures, a 4-substituted piperazine ring was formed by alkylation of the primary amino group of cyclohexane-derived amino alcs. with N,N-bis(2-chloroethyl)benzylamine. The hydroxylic group of the intermediate was first activated with methanesulfonyl chloride, and the sulfonic ester formed in situ was introduced into the reaction with the sodium salt of 1,2,4-triazole. In one case (i.e., preparation of I) introduction of the 1,2,4-triazole moiety was performed at a carbon of the cyclohexane ring. In addition, this intermediate contained a piperazine moiety connected via its nitrogen atom to a cyclohexane ring carbon neighboring the reaction center. As established in NMR and X-ray investigations, this substitution proceeded with retention of the initial trans configuration of 1,2-disubstituted cyclohexane. To obtain pure enantiomers of I, its precursor was subjected to chiral chromatog. on a Chirobiotic V column. The separated derivs. were introduced into further synthesis steps, giving (R,R)-I and (S,S)-I, resp. **Melanocortin** MC1,3-5 receptor binding studies showed that all tested piperazine derivs. were active. Several compds. showed clear selectivity for MC4R, with submicromolar affinities being obtained. (R,R)-I, displayed a biphasic curve in displacement of [125I]NDP-MSH on MC4R [K(i)high = 1 nM and K(i)low = 260 nM]. This biphasic competition curve was similarly biphasic to the competition curve obtained using THIQ. An X-ray study performed on crystals of THIQ sulfate revealed two closely related conformations, which resemble the shape of the letter Y, where piperidine and 4-chlorophenyl groups are situated close to each other, but the 1,2,3,4-tetrahydroisoquinoline residue is remote, the triazole function being highly exposed to the environment. The crystals of the dinitrate salt of (R,R)-I showed a different conformation, where parts of the mol. are spread out almost sym. around the central section. Mol. modeling, based on the THIQ crystal structure and the functional similarity of THIQ and (R,R)-I, led to a possible bioactive conformation of (R,R)-I that is

similar to the crystal conformation of THIQ.
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34
ST piperazine THIQ analog prepn **melanocortin** receptor ligand
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 766550-50-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 766550-06-5P 766550-08-7P **766550-12-3P 766550-14-5P**
766550-45-2P 766550-47-4P 766550-53-2P 766550-55-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 766550-36-1P 766550-37-2P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 55-51-6, N-Benzyl-N,N-bis(2-chloroethyl)amine 100-11-8 288-88-0, 1H-1,2,4-Triazole 2756-85-6, 1-Aminocyclohexanecarboxylic acid 5456-63-3, trans-2-Aminocyclohexanol hydrochloride 5691-20-3, cis-2-Aminocyclohexanecarboxylic acid 10316-79-7, 1-Aminocyclopentanemethanol 57292-44-1 115962-35-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 92-54-6P, 1-Phenylpiperazine 5460-68-4P 5691-15-6P, cis-2-Aminocyclohexanemethanol 5691-37-2P 17766-28-8P, 1-Cyclohexylpiperazine 187610-67-9P 213672-64-1P 252008-71-2P 511538-97-9P 668980-39-0P 766550-02-1P 766550-03-2P 766550-04-3P 766550-05-4P **766550-09-8P 766550-10-1P** 766550-15-6P 766550-16-7P 766550-17-8P 766550-18-9P 766550-19-0P 766550-20-3P 766550-21-4P 766550-22-5P 766550-23-6P 766550-24-7P 766550-25-8P 766550-26-9P 766550-27-0P 766550-28-1P 766550-29-2P 766550-31-6P 766550-33-8P 766550-35-0P 766550-39-4P 766550-40-7P 766550-41-8P 766550-42-9P 766550-43-0P 766550-44-1P 766550-56-5P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT 148893-10-1
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
IT **766550-12-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; **PREP (Preparation)**
(preparation of new substituted piperazines related to THIQ as ligands for **melanocortin** receptors)
RN 766550-12-3 HCAPLUS
CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-(4-oxido-4-phenyl-1-piperazinyl)-2-oxoethyl]-1,2,3,4-tetrahydro-, (3R)-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

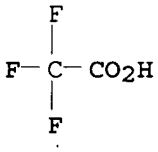
CRN 766550-11-2
CMF C29 H31 Cl N4 O3

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:370912 HCAPLUS
DN 140:407110
TI Preparation of piperazine amino acid derivatives and related compounds as **melanocortin** receptor ligands
IN Ebetino, Frank Hallock; Tian, Xinrong; Mazur, Wieslaw Adam; Colson, Anny-Odile
PA The Procter & Gamble Company, USA; Procter & Gamble
SO PCT Int. Appl., 265 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004037797	A2	20040506	WO 2003-US33402	20031022
	WO 2004037797	A3	20041104		

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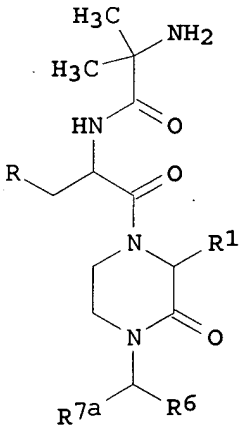
TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US	2005010031	A1	20050113	US 2003-689022	20031020
US	7132539	B2	20061107		
CA	2501231	A1	20040506	CA 2003-2501231	20031022
AU	2003286557	A1	20040513	AU 2003-286557	20031022
EP	1556361	A2	20050727	EP 2003-777759	20031022
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR	2003015614	A	20050830	BR 2003-15614	20031022
CN	1703221	A	20051130	CN 2003-80100934	20031022
JP	2006506384	T	20060223	JP 2004-546990	20031022
ZA	2005002944	A	20060222	ZA 2005-2944	20050412
NO	2005002476	A	20050523	NO 2005-2476	20050523
US	2006247224	A1	20061102	US 2006-473972	20060623
PRAI US	2002-420578P	P	20021023		
US	2003-689022	A3	20031020		
WO	2003-US33402	W	20031022		

OS MARPAT 140:407110

GI



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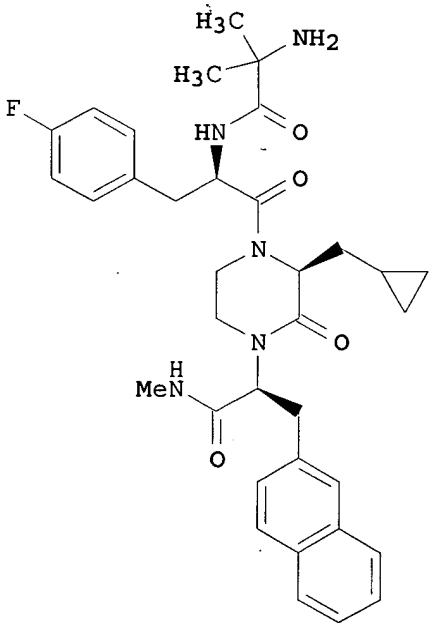

II

AB The invention relates to compds. which comprise a nitrogen-containing ring scaffold, e.g., 2-keto-3-alkylpiperazines I [R is Ph, 3- or 4-fluoro-, 3,5-difluoro- or 4-chlorophenyl; R1 is Me, Et, Pr, iso-Pr, Bu, iso-Bu, sec-Bu, tert-Bu, cyclopropyl, cyclopropylmethyl, cyclopentyl, cyclopentylmethyl, cyclohexyl, cyclohexylmethyl, benzyl, allyl, 1- or 2-methylallyl, but-2-enyl or propargyl; R7a is H, CO2H, CONH2, CONHMe, and -CONMe2, etc.; R8 is (un)substituted benzyl or naphthalen-2-ylmethyl], which are **melanocortin** receptor ligands. Thus, piperazinone derivative II was prepared via sequential peptide couplings in solution; the piperazine ring was formed by cyclocondensation of the allylglycinamide

moiety with 1,2-dibromoethane (K2CO3/DMF at 65° for 12 h).
IC ICM C07D241-00
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 63
ST piperazine amino acid prepn **melanocortin** receptor ligand
IT Muscle, disease
(atrophy; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Artery, disease
(coronary; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Learning
(deficiency; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Blood pressure
(elevated; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Embryo, animal
(fetus, intrauterine fetal growth; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Nerve
(growth and repair; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Ovarian cycle
(irregularities; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Diabetes mellitus
(non-insulin-dependent; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Sexual behavior
(penile erection; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Anti-inflammatory agents
Antiarthritics
Antihypertensives
Antiobesity agents
Antitumor agents
Cardiovascular system, disease
Fertility disorders
Gallbladder, disease
Gout
Hirsutism
Hypertension
Inflammation
Lung, disease
Neoplasm
Obesity
Osteoarthritis
Sepsis
Sexual disorders
Shock (circulatory collapse)
Sleep apnea
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT Dyslipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT Amino acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT Embolism
(thromboembolism; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT 50-99-7, Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intolerance; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT **686338-51-2P 686338-96-5P 686339-38-8P**
686340-85-2P 686340-87-4P 686753-58-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT 51293-47-1P 123929-73-7P **686336-96-9P 686336-97-0P**
686336-99-2P 686337-10-0P 686337-11-1P
686337-14-4P 686337-15-5P 686337-16-6P
686337-17-7P 686337-18-8P 686337-19-9P
686337-20-2P 686337-21-3P 686337-22-4P
686337-23-5P 686337-24-6P 686337-25-7P
686337-27-9P 686337-28-0P 686337-29-1P
686337-30-4P 686337-31-5P 686337-33-7P
686337-34-8P 686337-35-9P 686337-36-0P
686337-37-1P 686337-38-2P 686337-39-3P
686337-40-6P 686337-41-7P 686337-42-8P
686337-43-9P 686337-44-0P 686337-45-1P
686337-46-2P 686337-47-3P 686337-48-4P
686337-49-5P 686337-50-8P 686337-51-9P
686337-52-0P 686337-53-1P 686337-54-2P
686337-55-3P 686337-56-4P 686337-57-5P
686337-58-6P 686337-59-7P 686337-60-0P
686337-61-1P 686337-62-2P 686337-63-3P
686337-64-4P 686337-65-5P 686337-66-6P
686337-68-8P 686337-70-2P 686337-72-4P
686337-74-6P 686337-75-7P 686337-76-8P
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686337-80-4P 686337-81-5P 686337-87-1P
686337-89-3P 686337-90-6P 686337-91-7P
686337-92-8P 686337-93-9P 686337-94-0P
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686338-09-0P 686338-13-6P 686338-14-7P
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686338-43-2P 686338-47-6P 686338-53-4P
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686338-68-1P 686338-70-5P 686338-71-6P
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686338-95-4P 686338-98-7P 686338-99-8P
686339-00-4P 686339-02-6P 686339-03-7P
686339-04-8P 686339-05-9P 686339-06-0P
686339-07-1P 686339-08-2P 686339-09-3P
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686339-28-6P 686339-29-7P 686339-30-0P
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686339-37-7P 686339-39-9P 686339-40-2P
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686339-47-9P 686339-48-0P 686339-49-1P
686339-50-4P 686339-51-5P 686339-52-6P
686339-53-7P 686339-54-8P 686339-55-9P
686339-56-0P 686339-57-1P 686339-58-2P
686339-59-3P 686339-60-6P 686339-61-7P
686339-67-3P **686339-77-5P 686339-78-6P**
686339-79-7P 686339-80-0P 686339-81-1P
686339-82-2P 686339-83-3P 686339-84-4P
686339-85-5P 686339-86-6P 686339-87-7P
686339-88-8P 686339-89-9P 686339-91-3P
686339-94-6P 686339-97-9P 686339-98-0P
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686340-02-3P 686340-03-4P 686340-04-5P
686340-05-6P 686340-06-7P 686340-07-8P
686340-08-9P 686340-09-0P 686340-10-3P
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686340-14-7P 686340-15-8P 686340-16-9P
686340-17-0P 686340-18-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT **686340-19-2P 686340-20-5P 686340-21-6P**
686340-22-7P 686340-23-8P 686340-24-9P
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686340-43-2P 686340-44-3P 686340-45-4P
686340-46-5P 686340-47-6P 686340-48-7P
686340-49-8P 686340-50-1P 686340-51-2P

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686340-67-0P 686340-68-1P 686340-69-2P
686340-70-5P 686340-71-6P 686340-72-7P
686340-73-8P 686340-74-9P 686340-75-0P
686340-76-1P 686340-77-2P 686340-78-3P
686340-79-4P 686340-80-7P 686340-81-8P
686340-82-9P 686340-83-0P 686340-84-1P
686340-86-3P 686340-88-5P 686340-89-6P
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686753-23-1P 686753-24-2P 686753-25-3P
686753-26-4P 686753-27-5P 686753-28-6P
686753-29-7P 686753-31-1P 686753-32-2P
686753-33-3P 686753-34-4P 686753-35-5P
686753-36-6P 686753-37-7P 686753-38-8P
686753-39-9P 686753-40-2P 686753-42-4P
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686753-64-0P 686753-65-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT 98-79-3, L Pyroglutamic acid 106-93-4, 1 2 Dibromoethane 625-45-6, 2 Methoxyacetic acid 2799-21-5, 3 r Hydroxypyrrolidine 15761-39-4 22059-21-8, 1 Aminocyclopropanecarboxylic acid 30992-29-1 51077-14-6 57292-44-1 57292-45-2 88950-64-5 90600-20-7 102735-53-5 109063-69-6 151838-62-9 **686337-86-0** 686339-92-4 **686339-93-5 686339-95-7 686339-96-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT 109431-87-0P 686336-88-9P 686336-89-0P 686336-90-3P 686336-91-4P 686336-92-5P **686336-93-6P 686336-94-7P**
686336-95-8P 686336-98-1P 686337-00-8P 686337-01-9P 686337-02-0P **686337-03-1P 686337-04-2P**
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686337-12-2P 686337-83-7P 686337-84-8P
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686338-06-7P 686338-08-9P 686338-10-3P
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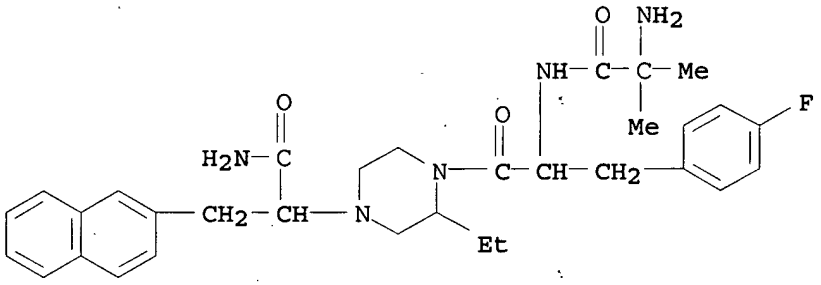
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance; preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
IT **686338-51-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses) (preparation of piperazine amino acid derivs. and related compds. as **melanocortin** receptor ligands)
RN 686338-51-2 HCAPLUS
CN 1-Piperazineacetamide, 3-ethyl-4-(2-methylalanyl-4-fluorophenylalanyl)-α-(2-naphthalenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

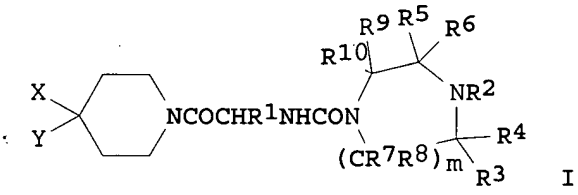
L35 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:252507 HCAPLUS
DN 140:287409
TI Preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists
IN Bakshi, Raman Kumar; Nargund, Ravi P.; Palucki, Brenda L.; Park, Min K.; Ye, Zhixiong
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004024720	A1	20040325	WO 2003-US27892	20030905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498272	A1	20040325	CA 2003-2498272	20030905

	AU 2003268493	A1	20040430	AU 2003-268493	20030905
	EP 1539735	A1	20050615	EP 2003-749459	20030905
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006505531	T	20060216	JP 2004-536116	20030905
	US 2006040906	A1	20060223	US 2005-526178	20050228
PRAI	US 2002-409879P	P	20020911		
	WO 2003-US27892	W	20030905		

OS MARPAT 140:287409

GI



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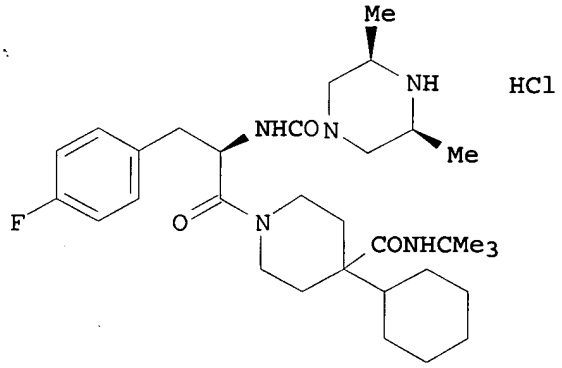

II

AB Piperazines I [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, heteroaryl; R2 = H, (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl, heteroaryl, CH2C.tplbond.CH, CH2CHF2; R3-R10 = H, (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl, heteroaryl; R3R5, R3R9, R5R7, R7R9 = atoms required to complete a 5-7-membered ring; X = (un)substituted alkyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, CN, CONH2, CO2H, acyl, NH2, SH, s(O)H, SO2H, OH; Y = H, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl; m = 1, 2] were prepared for use as agonists of the human **melanocortin**-4 receptor (MC-4R) and, in particular, as receptor-subtype selective agonists of MC-4R. They are useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity and diabetes. Thus, (R)-4-FC6H4CH2CH(CO2H)NHCO2CMe3 was treated with 1-cyclohexyl-4-tert.-butoxycarbamoylpiperidine hydrochloride, followed by deblocking and reaction with cis-2,6-dimethylpiperazine to give the title compound II.

IC ICM C07D401-12
ICS C07D403-12; A61K031-453; A61K031-4545; A61P003-04; A61P003-10

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST carbamoylpiperazine prepn **melanocortin** receptor agonist

IT Heart, disease

(arrhythmia; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Hypertrophy
(cardiac; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Intestine, neoplasm
(colon; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Artery, disease
(coronary; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Uterus, neoplasm
(endometrium; preparation of carbamoylpiperazines as **melanocortin** -4 receptor agonists)
IT Heart, disease
(failure; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Digestive tract, disease
(gastroesophageal reflux; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Eating disorders
(hyperphagia; preparation of carbamoylpiperazines as **melanocortin** -4 receptor agonists)
IT Heart, disease
(hypertrophy; preparation of carbamoylpiperazines as **melanocortin** -4 receptor agonists)
IT Reproductive system, disease
(hypogonadism; preparation of carbamoylpiperazines as **melanocortin** -4 receptor agonists)
IT Heart, disease
(infarction; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)
IT Ovary, disease
(polycystic; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists).
IT Anti-inflammatory agents
Antiarthritics
Anticholesteremic agents
Antihypertensives
Antitumor agents
Arteriosclerosis
Bulimia
Calculi, biliary
Cardiovascular system, disease
Diabetes mellitus
Fertility disorders
Gallbladder, disease
Gout
Heart, disease
Hirsutism
Human
Hypercholesterolemia
Hypertension
Inflammation
Kidney, neoplasm
Mammary gland, neoplasm

Obesity
Osteoarthritis
Prader-Willi syndrome
Prostate gland, neoplasm
Reproduction disorders
Sexual disorders
Sleep apnea
Turner syndrome
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT Dyslipidemia
Hyperlipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT Growth disorders, animal
(short stature; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT Brain, disease
(stroke; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT Death
(sudden death; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 9002-72-6, Somatotropin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(deficiency; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 69-93-2, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperuricemia; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 674791-30-1P 674791-38-9P 674791-48-1P 674791-50-5P 674791-54-9P
674792-30-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 674790-45-5P 674790-46-6P 674790-47-7P 674790-48-8P 674790-49-9P
674790-50-2P 674790-51-3P 674790-52-4P 674790-53-5P 674790-54-6P
674790-55-7P 674790-56-8P 674790-57-9P 674790-58-0P 674790-59-1P
674790-60-4P 674790-61-5P 674790-62-6P 674790-63-7P 674790-64-8P
674790-65-9P 674790-66-0P 674790-67-1P 674790-68-2P 674790-69-3P
674790-70-6P 674790-71-7P 674790-72-8P 674790-73-9P 674790-74-0P
674790-75-1P 674790-76-2P 674790-77-3P 674790-78-4P 674790-79-5P
674790-80-8P **674790-81-9P** **674790-82-0P**
674790-83-1P **674790-84-2P** **674790-85-3P**
674790-86-4P **674790-87-5P** 674790-88-6P 674790-89-7P
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674791-05-0P 674791-06-1P 674791-07-2P 674791-08-3P
674791-09-4P 674791-10-7P 674791-11-8P 674791-12-9P
674791-13-0P **674791-14-1P** **674791-15-2P**
674791-16-3P **674791-17-4P** **674791-18-5P**
674791-19-6P 674791-20-9P 674791-21-0P 674791-22-1P
674791-23-2P 674791-24-3P 674791-25-4P 674791-26-5P 674791-27-6P
674791-28-7P 674791-29-8P 674791-31-2P 674791-32-3P 674791-33-4P
674791-34-5P 674791-35-6P 674791-36-7P 674791-37-8P 674791-39-0P

674791-40-3P 674791-41-4P 674791-43-6P 674791-44-7P 674791-45-8P
674791-46-9P 674791-47-0P 674791-49-2P 674791-51-6P 674791-52-7P
674791-53-8P 674791-55-0P 674791-56-1P 674791-58-3P 674791-59-4P
674791-60-7P 674791-61-8P 674791-63-0P 674791-65-2P 674791-67-4P
674791-68-5P 674792-28-0P 674792-31-5P 674792-32-6P 674792-33-7P
674792-34-8P 674792-35-9P 674792-36-0P 674792-37-1P 674792-38-2P
674792-39-3P 674792-40-6P 674792-41-7P 674792-42-8P 674792-43-9P
674792-44-0P 674792-45-1P 674792-46-2P 674792-47-3P 674792-48-4P
674792-49-5P 674792-50-8P 674792-51-9P 674792-52-0P 674792-53-1P
674792-54-2P 674792-55-3P 674792-56-4P 674792-57-5P 674792-58-6P
674792-59-7P 674792-60-0P 674792-61-1P 674792-62-2P 674792-63-3P
674792-64-4P 674792-66-6P **674792-68-8P 674792-70-2P**
674792-72-4P 674792-73-5P 674792-75-7P
674792-77-9P 674792-78-0P 674792-79-1P 674792-80-4P
674792-81-5P 674792-82-6P 674792-83-7P 674792-85-9P 674792-86-0P
674792-87-1P 674792-88-2P 674792-89-3P 674792-90-6P 674792-91-7P
674792-92-8P 674792-93-9P 674792-94-0P 674792-96-2P 674792-98-4P
674792-99-5P 674793-00-1P 674793-03-4P 674793-05-6P
674793-07-8P 674793-09-0P 674793-11-4P 674793-13-6P 674793-16-9P
674793-18-1P 674793-20-5P 674793-22-7P 674793-24-9P 674798-14-2P
675832-45-8P 675832-46-9P 675832-47-0P 675832-48-1P 675832-49-2P
675832-50-5P 675832-51-6P 675832-52-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 104-63-2, N-Benzylethanolamine 105-45-3, Methyl acetoacetate 105-56-6, Ethyl cyanoacetate 124-68-5, 2-Amino-2-methyl-1-propanol 279-40-3, 7-Azabicyclo[2.2.1]heptane 625-36-5, 3-Chloropropionyl chloride 931-51-1, Cyclohexylmagnesium chloride 1124-11-4, Tetramethylpyrazine 2081-44-9 2749-11-3, (S)-2-Amino-1-propanol 4300-97-4, 3-Chloropivaloyl chloride 4635-59-0, 4-Chlorobutyryl chloride 4774-14-5, 2,6-Dichloropyrazine 7764-95-6, N-tert.-Butoxycarbonyl-D-alanine 10316-79-7, 1-Amino-1-cyclopentanemethanol 13139-15-6, N-tert.-Butoxycarbonyl-L-leucine 13734-41-3, N-tert.-Butoxycarbonyl-L-valine 15761-38-3, N-tert.-Butoxycarbonyl-L-alanine 21655-48-1, cis-2,6-Dimethylpiperazine 22059-21-8, 1-Amino-1-cyclopropanecarboxylic acid 22838-58-0, N-tert.-Butoxycarbonyl-D-valine 26250-84-0 27871-49-4, Methyl (S)-lactate 28697-17-8 30992-29-1, N-tert.-Butoxycarbonyl-2-methylalanine 34306-42-8 45121-22-0 57292-45-2 79099-07-3, N-tert.-Butoxycarbonyl-4-piperidinone 88950-64-5, N-tert.-Butoxycarbonyl-1-aminocyclopropane-1-carboxylic acid 181641-61-2 312638-87-2 312638-89-4 312638-96-3 363191-00-8 674791-75-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT 867-13-0P 6135-46-2P 13067-27-1P 74474-93-4P 132871-12-6P
162150-51-8P 162150-52-9P 162240-92-8P 162240-93-9P 169447-69-2P
169447-70-5P 170033-54-2P 170033-57-5P 170211-03-7P 193537-11-0P
273378-16-8P 324748-62-1P 324750-04-1P 325145-35-5P 363191-01-9P
363191-02-0P 363191-03-1P 363191-04-2P 363192-22-7P 363192-23-8P
363192-24-9P 363192-25-0P 363192-26-1P 363192-27-2P 363192-28-3P
363192-29-4P 363192-30-7P 363192-31-8P 363192-32-9P 363192-33-0P
363192-34-1P 363192-35-2P 363192-38-5P 444891-95-6P 444892-01-7P
444892-03-9P 455954-48-0P 455954-49-1P 455954-50-4P 455954-51-5P
455954-52-6P 455954-53-7P 455954-54-8P 455954-55-9P 455954-56-0P
455954-57-1P 455954-58-2P 455954-59-3P 455954-60-6P 455954-61-7P
455954-62-8P 455954-63-9P 455954-64-0P 455954-65-1P 455954-66-2P

455954-67-3P 455954-68-4P 455954-69-5P 455954-70-8P 455954-71-9P
455954-72-0P 455954-73-1P 455954-74-2P 455954-75-3P 455954-76-4P
455954-77-5P 455954-78-6P 502482-44-2P 527706-30-5P 634922-12-6P
635303-45-6P 674791-69-6P 674791-70-9P 674791-71-0P 674791-72-1P
674791-73-2P 674791-74-3P 674791-76-5P 674791-77-6P 674791-78-7P
674791-79-8P 674791-80-1P 674791-81-2P 674791-82-3P 674791-83-4P
674791-84-5P 674791-85-6P 674791-86-7P 674791-87-8P 674791-88-9P
674791-89-0P 674791-90-3P 674791-91-4P 674791-92-5P 674791-93-6P
674791-94-7P 674791-95-8P 674791-96-9P 674791-97-0P 674791-98-1P
674791-99-2P 674792-00-8P 674792-01-9P 674792-02-0P 674792-03-1P
674792-04-2P 674792-05-3P 674792-06-4P 674792-07-5P 674792-08-6P
674792-09-7P 674792-10-0P 674792-11-1P 674792-12-2P 674792-13-3P
674792-14-4P 674792-15-5P 674792-16-6P 674792-17-7P 674792-18-8P
674792-19-9P 674792-20-2P 674792-21-3P 674792-22-4P 674792-23-5P
674792-24-6P 674792-25-7P 674792-26-8P 674792-27-9P 674792-29-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

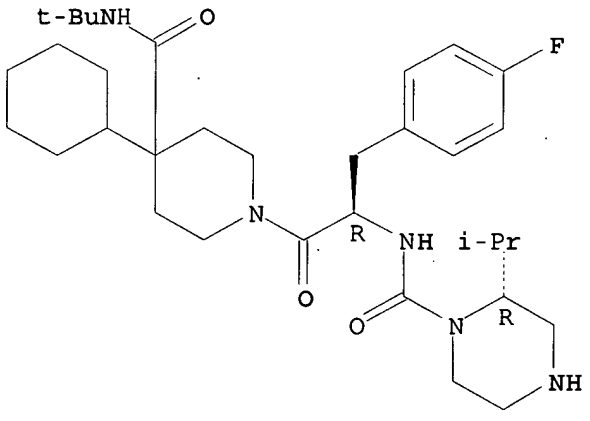
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

IT **674790-81-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of carbamoylpiperazines as **melanocortin**-4 receptor agonists)

RN 674790-81-9 HCAPLUS

CN 1-Piperazinecarboxamide, N-[(1R)-2-[4-cyclohexyl-4-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperidinyl]-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-2-(1-methylethyl)-, monohydrochloride, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:2850 HCAPLUS
DN 140:77013
TI Preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia
IN Jaehne, Gerhard; Frick, Wendelin; Flohr, Stefanie; Lindenschmidt, Andreas; Glombik, Heiner; Kramer, Werner; Heuer, Hubert; Schaefer, Hans-Ludwig
PA Aventis Pharma Deutschland G.m.b.H., Germany
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004000804	A1	20031231	WO 2003-EP5815	20030604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10227506	A1	20040108	DE 2002-10227506	20020619
CA 2490109	A1	20031231	CA 2003-2490109	20030604
AU 2003242616	A1	20040106	AU 2003-242616	20030604
EP 1517892	A1	20050330	EP 2003-760591	20030604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003011940	A	20050405	BR 2003-11940	20030604
CN 1662493	A	20050831	CN 2003-814087	20030604
NZ 537304	A	20051028	NZ 2003-537304	20030604
JP 2005533072	T	20051104	JP 2004-514660	20030604
US 2004082561	A1	20040429	US 2003-463807	20030618
NO 2005000073	A	20050106	NO 2005-73	20050106
US 2006270613	A1	20061130	US 2006-501758	20060810
PRAI DE 2002-10227506	A	20020619		
US 2002-411984P	P	20020919		
WO 2003-EP5815	W	20030604		
US 2003-463807	A1	20030618		

OS MARPAT 140:77013
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2, R3, R4, R5, R6 = (un)substituted alkylene-(LAG)n; n = 1-5; LAG = sugar; amino sugar; amino acid, etc.] and their pharmaceutically acceptable salts were prepared For example, N-alkylation of 1,4-diazabicyclo[2.2.2]octane with benzyl bromide II, e.g., prepared from 1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-(4-hydroxyphenyl)-2-azetidinone and 1,2-bisbromomethylbenzene, afforded diphenylazetidinone III. In rat liver chloresterol absorption assays, 26-examples of compds. I exhibited EC50 values ranging from 0.03-<1.0

(mg/mouse), e.g., the EC50 value of diphenylazetidinone III was 0.3. Compds. I are claimed useful for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia.

IC ICM C07D205-08
ICS A61K031-397; A61P003-06

CC 27-5 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST antiarteriosclerotic agent prepn diphenylazetidinone chloresterol absorption; anticholesteremic agent prepn diphenylazetidinone chloresterol absorption; antilipidemic agent prepn diphenylazetidinone chloresterol absorption

IT 5-HT antagonists
(5-HT1, medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AP-2 (activator protein 2), medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Histones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Lipoprotein receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Lp(a), medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MTP (microsomal triglyceride-exchanging protein), medicaments with inhibitors of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(amylase-inhibiting, medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol ester-exchanging, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of α/γ; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Bombesin receptors
Cocaine receptors
Galanin receptors
Growth hormone secretagogue receptors
Neuropeptide Y receptors
Retinoid X receptors

Thyroid hormone receptors
Thyrotropin-releasing hormone receptors
Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Adrenoceptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Bile acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with resorption inhibitors and polymeric adsorbents of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 5-HT antagonists
5-HT reuptake inhibitors
Antidiabetic agents
Antioxidants
Peroxisome proliferators
β-Adrenoceptor antagonists
β3-Adrenoceptor agonists
(medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT MSH receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Antiarteriosclerotics
Anticholesteremic agents
Human
Hypolipemic agents
(preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Lipid metabolism
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of disorders; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Arteriosclerosis
Hypercholesterolemia
(treatment of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Hyperlipidemia
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 439080-60-1P 639504-72-6P 640334-24-3P 640334-52-7P 640335-29-1P 640335-37-1P 640335-47-3P 640335-51-9P 640335-57-5P 640335-62-2P 640335-72-4P 640335-77-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 560976-56-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 9002-72-6, Somatotropin 9011-97-6, CCK 9015-71-8, CRF 169494-85-3, Leptin 193830-48-7, Urocortin 245359-74-4, Orexin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with agonist of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 9001-42-7, α-Glucosidase 9001-62-1, Lipase 9004-02-8, Lipo protein lipase 9027-63-8, Cholesterol acyltransferase 9027-95-6, ATP-citrate lyase 9077-14-9, Squalene synthetase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with inhibitors of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 57-88-5, Cholesterol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with lowering drugs and resorption inhibitors of; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 56-03-1, Biguanide 300-62-9, Amphetamine 2295-31-0, Thiazolidinedione 9004-10-8, Insulin, biological studies 25614-03-3, Bromocriptine 54870-28-9, Meglitinide 129024-87-9, Doprexin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 91-13-4, 1,2-Bisbromomethylbenzene 100-76-5, 1-Azabicyclo[2.2.2]octane 106-58-1, 1,4-Dimethylpiperazine 109-02-4, n-Methylmorpholine 280-57-9, Dabco 488-43-7, D-Glucamine 623-24-5, 1,4-Bisbromomethylbenzene 626-15-3, 1,3-Bisbromomethylbenzene 790-83-0 2215-89-6 3230-39-5, 4-[(4-Methoxybenzylidene)amino]phenol 3381-48-4 13737-36-5 18162-48-6, tert-Butyldimethylsilyl chloride 20248-86-6, 4,4'-Bisbromomethylbiphenyl 20256-89-7, 4-[(4-Methoxyphenylimino)-methyl]benzonitrile 22257-39-2 60537-19-1, 2,3,4,5,6-Pentahydroxyhexylamine 90191-92-7, 6-Methylamino-1,2,3,4,5-hexanol 96556-05-7, 1,4,7-Trimethyl[1,4,7]triazonane 640334-30-1 640334-65-2 640335-17-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 439080-20-3P 439080-21-4P 439080-61-2P 439080-62-3P 638213-19-1P 639504-75-9P 640334-81-2P 640334-86-7P 640334-91-4P 640334-97-0P 640335-05-3P 640335-11-1P 640335-26-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

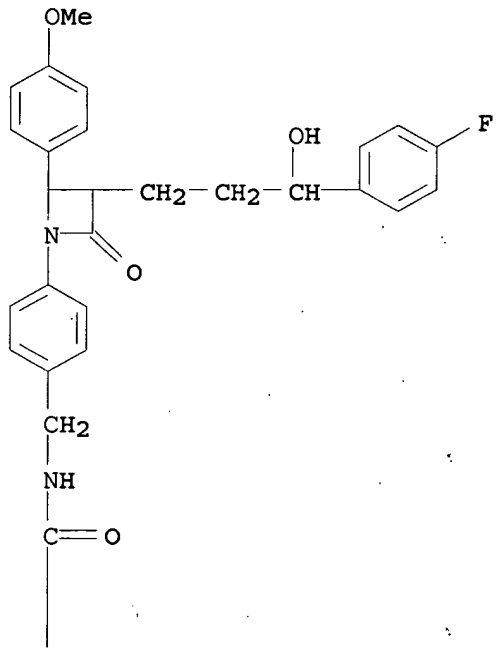
IT 439081-02-4
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

IT 640330-69-4P 640330-76-3P 640330-84-3P 640330-96-7P 640331-07-3P
640331-17-5P 640331-26-6P 640331-33-5P 640331-40-4P 640331-48-2P
640331-55-1P 640331-63-1P 640331-70-0P 640331-76-6P 640331-81-3P
640331-86-8P 640331-93-7P 640332-06-5P 640332-27-0P 640332-35-0P
640332-41-8P 640332-52-1P 640332-61-2P 640332-67-8P 640332-73-6P
640332-81-6P 640332-86-1P **640332-92-9P 640332-97-4P**
640333-03-5P 640333-11-5P 640333-18-2P 640333-25-1P 640333-31-9P
640333-38-6P 640333-42-2P 640333-46-6P 640333-50-2P
640333-56-8P 640333-69-3P 640333-74-0P 640333-80-8P 640333-85-3P
640333-90-0P 640333-96-6P 640334-02-7P 640334-08-3P
640334-14-1P 640334-18-5P 641614-30-4P 641614-31-5P 641614-32-6P
641614-33-7P 641614-34-8P 641614-35-9P 641614-36-0P 641614-37-1P
641614-38-2P 641614-39-3P 641614-40-6P 641614-41-7P 641614-42-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(target compound; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

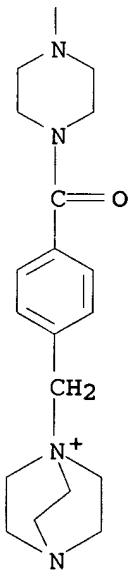
IT **640332-92-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(target compound; preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis and hypercholesterolemia)

RN 640332-92-9 HCAPLUS
CN 4-Aza-1-azoniabicyclo[2.2.2]octane, 1-[[4-[[4-[[[[4-[3-[3-(4-fluorophenyl)-3-hydroxypropyl]-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]methyl]amino]carbonyl]-1-piperazinyl]carbonyl]phenyl]methyl]-, chloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



● Cl⁻

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:2849 HCAPLUS
DN 140:77012

TI Preparation of diphenylazetidinones for the treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia

IN Jaehne, Gerhard; Frick, Wendelin; Flohr, Stefanie; Lindenschmidt, Andreas; Glombik, Heiner; Kramer, Werner; Heuer, Hubert; Schaefer, Hans-ludwig

PA Aventis Pharma Deutschland GmbH, Germany

SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004000803	A1	20031231	WO 2003-EP5814	20030604
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10227507	A1	20040108	DE 2002-10227507	20020619
	CA 2490108	A1	20031231	CA 2003-2490108	20030604
	AU 2003238209	A1	20040106	AU 2003-238209	20030604
	EP 1517890	A1	20050330	EP 2003-735534	20030604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003011984	A	20050426	BR 2003-11984	20030604
	CN 1662494	A	20050831	CN 2003-814093	20030604
	JP 2005533071	T	20051104	JP 2004-514659	20030604
	NZ 537303	A	20060630	NZ 2003-537303	20030604
	US 2004077623	A1	20040422	US 2003-463789	20030618
	NO 2005000088	A	20050106	NO 2005-88	20050106
PRAI	DE 2002-10227507	A	20020619		
	US 2002-411981P	P	20020919		
	WO 2003-EP5814	W	20030604		

OS MARPAT 140:77012

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2, R3, R4, R5, R6 = (un)substituted alkylene-(LAG)n; n = 1-5; LAG = sugar; amino sugar; amino acid, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation of benzonitrile II e.g., prepared from 3-[5-(4-fluorophenyl)-5-hydroxypentanoyl]-4-phenyloxazolidin-2-one in 4-steps, and hydroxylamine hydrochloride afforded N-hydroxybenzenecarboximidamide III. In rat liver cholesterol absorption assays, 14-examples of compds. I exhibited EC50 values ranging from 0.03-<1.0 (mg/mouse), e.g., the EC50 value of N-hydroxybenzenecarboximidamide III was 0.1. Compds. I are claimed useful for the treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia.

IC ICM C07D205-08
ICS C07D487-08; A61K031-397; A61P003-06; A61P009-10; C07D241-00

CC 27-5 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

ST anticholesteremic agent prepn diphenylazetidinone cholesterol absorption; antiarteriosclerotic agent prepn diphenylazetidinone cholesterol absorption; antilipidemic agent prepn diphenylazetidinone cholesterol absorption

IT Uncoupling protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2, receptor; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Uncoupling protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(3, receptor; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 5-HT antagonists
(5-HT1, medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AP-2 (activator protein 2), medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Histones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Lipoprotein receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LDL, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Lp(a), medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MTP (microsomal triglyceride-exchanging protein), medicaments with inhibitors of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(amylase-inhibiting, medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cholesterol ester-exchanging, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of α/γ; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Adrenoceptors
Bombesin receptors
Cocaine receptors
Galanin receptors

Growth hormone secretagogue receptors
Neuropeptide Y receptors
Retinoid X receptors
Thyroid hormone receptors
Thyrotropin-releasing hormone receptors
Tumor necrosis factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Bile acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with resorption inhibitors and polymeric adsorbents of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 5-HT antagonists
5-HT reuptake inhibitors
Antidiabetic agents
Antioxidants
Peroxisome proliferators
β-Adrenoceptor antagonists
β3-Adrenoceptor agonists
(medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT MSH receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Antiarteriosclerotics
Anticholesteremic agents
Human
Hypolipemic agents
(preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Lipid metabolism
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of disorders; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Arteriosclerosis
Hypercholesterolemia
(treatment of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Hyperlipidemia
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 439080-20-3P 439080-24-7P, 3-[5-(tert-Butyl-dimethylsilanyloxy)-5-(4-fluorophenyl)pentanoyl]-4-phenyloxazolidin-2-one 439080-60-1P, 4-[3-[3-(tert-Butyl-dimethylsilanyloxy)-3-(4-fluorophenyl)propyl]-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl]benzonitrile 439080-61-2P, 4-[3-[3-(4-Fluorophenyl)-3-hydroxypropyl]-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl]benzonitrile 638212-96-1P 639504-71-5P 639504-72-6P 639504-74-8P 639504-76-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 9002-72-6, Somatotropin 9011-97-6, Cholecystokinin 9015-71-8, Corticotropin-releasing factor 560976-56-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 169494-85-3, Leptin 193830-48-7, Urocortin 245359-74-4, Orexin (peptide)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with agonist of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 9001-42-7 9001-62-1 9004-02-8 9027-63-8 9027-95-6 9077-14-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(medicaments with inhibitors of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with lowering drugs and resorption inhibitors of; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 56-03-1, Imidodicarbonimidic diamide 300-62-9 2295-31-0, 2,4-Thiazolidinedione 9004-10-8, Insulin, biological studies 25614-03-3 54870-28-9 129024-87-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 280-57-9, 1,4-Diazabicyclo[2.2.2]octane 693-13-0, Diisopropylcarbodiimide 4224-70-8, 6-Bromohexanoic acid 5470-11-1, Hydroxylamine hydrochloride 18162-48-6, Tert-ButylDimethylsilylchloride 20256-89-7, 4-[(4-Methoxyphenylimino)methyl]benzonitrile 39769-21-6, 4-[(4-Fluorophenylimino)methyl]benzonitrile 73367-80-3, 12-Bromododecanoic acid 439080-96-3, 3-[5-(4-Fluorophenyl)-5-hydroxypentanoyl]-4-phenyloxazolidin-2-one 639504-73-7, 4-[3-[3-(4-Fluorophenyl)-3-hydroxypropyl]-2-(4-fluorophenyl)-4-oxoazetidin-1-yl]-benzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 639504-29-3P 639504-32-8P 639504-34-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

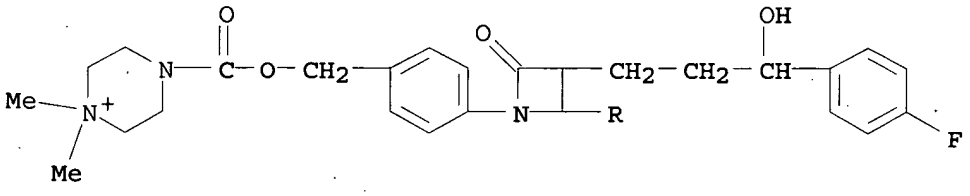
(target compound; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

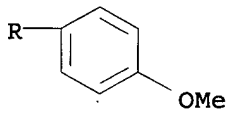
IT 439080-21-4, 4-(4-Aminomethylphenyl)-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]azetidin-2-one 639504-75-9, 1-(4-Aminomethylphenyl)-3-(3-hydroxy-3-phenylpropyl)-4-phenylazetidin-2-one 639504-77-1
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT 639504-31-7P 639504-33-9P 639504-35-1P 639504-37-3P 639504-39-5P
639504-41-9P 639504-43-1P 639504-45-3P 639504-46-4P 639504-47-5P
639504-49-7P 639504-50-0P 639504-51-1P 639504-52-2P 639504-53-3P
639504-54-4P 639504-55-5P 639504-56-6P **639504-57-7P**
639504-58-8P 639504-59-9P 639504-60-2P
639504-61-3P 639504-62-4P 639504-64-6P 639504-65-7P 639504-66-8P
639504-67-9P 639504-68-0P 639504-69-1P **639504-70-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(target compound; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

IT **639504-57-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(target compound; preparation of diphenylazetidinones for treatment of hyperlipidemia, arteriosclerosis, and hypercholesterolemia)

RN 639504-57-7 HCAPLUS
CN Piperazinium, 4-[[[4-[3-[3-(4-fluorophenyl)-3-hydroxypropyl]-2-(4-methoxyphenyl)-4-oxo-1-azetidinyl]phenyl]methoxy]carbonyl]-1,1-dimethyl-, iodide (9CI) (CA INDEX NAME)





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RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:1001971 HCAPLUS
DN 140:321326

TI Synthesis of novel **melanocortin** 4 receptor agonists and antagonists containing a succinamide core

AU Xi, Ning; Hale, Clarence; Kelly, Michael G.; Norman, Mark H.; Stec, Markian; Xu, Shimin; Baumgartner, James W.; Fotsch, Christopher

CS Department of Chemistry Research & Discovery, Amgen Inc., Thousand Oaks, CA, 91320, USA

SO Bioorganic & Medicinal Chemistry Letters (2004), 14(2), 377-381
CODEN: BMCLE8; ISSN: 0960-894X

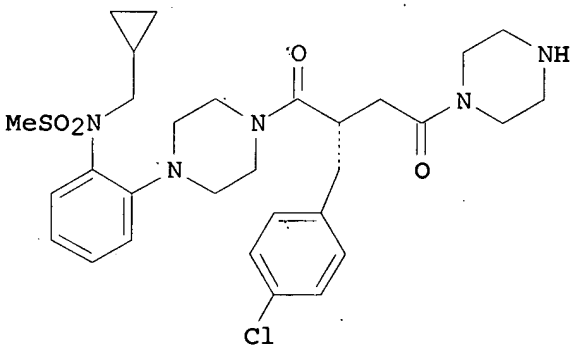
PB Elsevier Science B.V.

DT Journal

LA English

OS CASREACT 140:321326

GI



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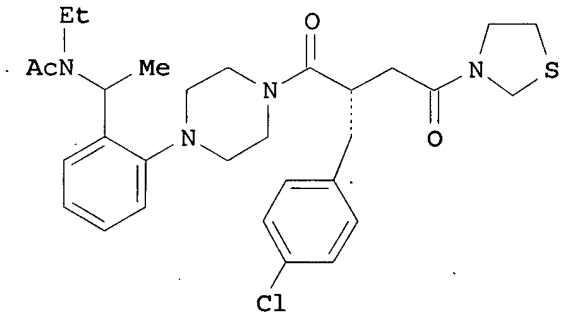


II

AB A novel series of piperazines appended to a succinamide backbone were synthesized and found to have a high affinity for the **melanocortin** -4 receptor (IC50s ranging from <0.1 to 200 nM). Both agonists and antagonists of MC4R were prepared by modifying the groups attached to the right-hand side of the succinamide. This series also exhibits a high level of selectivity (up to 7000-fold) over mouse MC1R and human MC3R. Example compds. included a piperazine succinamide analog (I) and thiazolidine succinamide analog (II).

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 75

ST **melanocortin** receptor agonist antagonist succinamide core analog prepn; piperazine **melanocortin** receptor agonist antagonist succinamide core analog prepn; thiazolidine piperazine **melanocortin** receptor agonist antagonist succinamide analog prepn; azetidine piperazine **melanocortin** receptor agonist antagonist

succinamide analog prepn; pyridine piperazine **melanocortin** receptor agonist antagonist succinamide analog prepn; structure activity **melanocortin** receptor agonist antagonist succinamide analog prepn; pituitary **melanocortin** receptor agonist antagonist succinamide analog prepn; human pituitary **melanocortin** receptor agonist antagonist succinamide analog prepn; crystal structure chlorophenylmethyl butanedioic acid dimethylethyl ester prepn; mol structure chlorophenylmethyl butanedioic acid dimethylethyl ester prepn

IT Human
(agonists and antagonists; preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 1, agonists and antagonists; preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3, agonists and antagonists; preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4, agonists and antagonists; preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT Structure-activity relationship
(**melanocortin** receptor agonistic and **melanocortin** receptor antagonistic; preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT Crystal structure
Molecular structure
(of [(chlorophenyl)methyl]butanedioic acid dimethylethyl ester)

IT **494783-55-0P** 678995-31-8P **678995-33-0P** **678995-35-2P** **678995-37-4P** **678995-39-6P** **678995-42-1P** **678995-44-3P** **678995-46-5P** **678995-48-7P** 678995-49-8P 678995-50-1P 678995-51-2P 678995-52-3P 678995-53-4P **678995-54-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT 75-04-7, Ethanamine, reactions 75-07-0, Acetaldehyde, reactions 75-36-5, Acetyl chloride 89-99-6, 2-Fluorobenzenemethanamine 98-88-4, Benzoyl chloride 123-38-6, Propanal, reactions 503-29-7, Azetidine 504-78-9, Thiazolidine 541-41-3, Ethyl chloroformate 590-86-3, Isopentanal 1489-69-6, Cyclopropanecarboxaldehyde 2516-34-9, Cyclobutanamine 3731-51-9, 2-Pyridinemethanamine 5292-43-3, tert-Butyl bromoacetate 7051-34-5, (Bromomethyl)cyclopropane 7065-46-5 24608-52-4, tert-Butyl chloroformate 52085-96-8, 4-Chlorobenzenepropanoyl chloride 57260-71-6, 1-Piperazinecarboxylic acid 1,1-dimethylethyl ester 102029-44-7, (4R)-4-(Phenylmethyl)-2-oxazolidinone 199105-18-5 626219-18-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT 494783-46-9P 494783-49-2P 494783-50-5P 494783-53-8P 494783-54-9P 678995-20-5P 678995-25-0P 678995-27-2P 678995-28-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

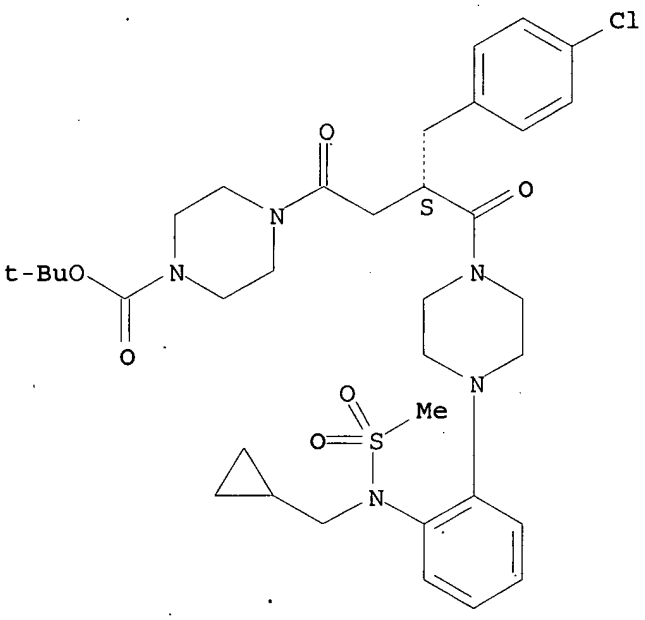
(preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

IT 494783-51-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core and study of crystal and mol. structures of [(chlorophenyl)methyl]butanedioic acid dimethylethyl ester)

IT **494783-55-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(preparation of **melanocortin** 4 receptor agonists and antagonists containing a succinamide core)

RN 494783-55-0 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[(3S)-3-[(4-chlorophenyl)methyl]-4-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]-1-piperazinyl]-1,4-dioxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

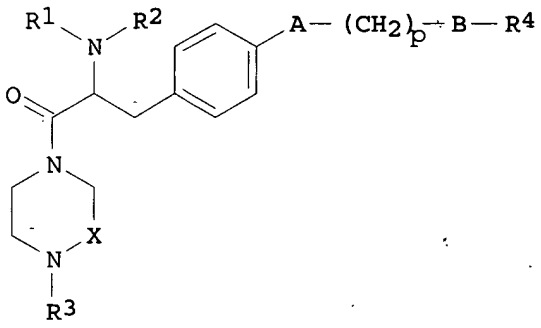


RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:991170 HCAPLUS
DN 140:42460
TI Preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivatives as **melanocortin** agonists
IN Poindexter, Graham S.; Luo, Guanglin; Chen, Ling
PA Bristol-Myers Squibb Company, USA
SO U.S. Pat. Appl. Publ., 53 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	US 2003232807	A1	20031218	US 2002-264709	20021004
	US 6916812	B2	20050712		
PRAI	US 2001-327961P	P	20011009		
OS	MARPAT 140:42460				
GI					



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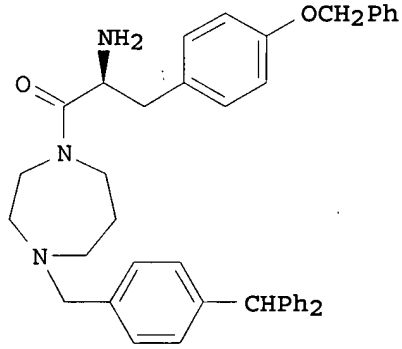

II

AB Novel piperazine and homopiperazine derivs. are agonists of **melanocortin** receptor(s) and are useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of the **melanocortin** receptors. Compds. I [X is CH2 or CH2CH2; p is 0-4; A is a bond or O; B is a bond, O, S, NH or alkylimino; R1, R2 are H, alkyl, phenylalkyl, imidazolylalkyl, imidazolylalkylcarbonyl, imidazolylcarbonyl, morpholinylalkyl, piperidinylalkyl, and dialkylaminoalkyl; R3 is alkyl or alkyl substituted by carbo- or heterocycles; R4 is (cyclo)alkyl, Ph, phenylalkyl, naphthalenyl, etc.] or pharmaceutically-acceptable salts are claimed. Thus, tyrosinamide derivative II was prepared by reductive amination/deprotection of N-(tert-butoxycarbonyl)-O-(phenylmethyl)-L-tyrosine 1-homopiperazinamide (preparation given) with p-benzhydrylbenzaldehyde. Compound II showed the following biol. activities: displacement rate 91-100% at 10 μM and MC4R IC50 <1.5 μM.

IC ICM A61K031-55
ICS A61K031-496; A61K031-551; A61K031-5377; C07D413-02; C07D043-02

INCL 514218000; 514235800; 514253010; 514253090; 514254010; 514254050; 514254080; 540575000; 544120000; 544360000

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28

ST aminoacyl piperazine homopiperazine prepn agonist **melanocortin**

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

IT Antidiabetic agents
Antiobesity agents
Obesity
Sexual disorders
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

IT **636605-31-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

IT **636606-82-1P 636606-83-2P 636606-84-3P**
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs. as **melanocortin** agonists)

IT 60-12-8, Phenethyl alcohol 64-17-5, Ethanol, reactions 66-77-3, 1 Naphthalenecarboxaldehyde 66-99-9, 2 Naphthalenecarboxaldehyde 67-36-7 67-63-0, Isopropyl alcohol, reactions 67-64-1, Acetone, reactions 71-23-8, 1 Propanol, reactions 71-36-3, 1 Butanol, reactions 78-84-2, Isobutyraldehyde 86-58-8 89-95-2 89-98-5 91-88-3 93-03-8, Benzenemethanol 3 4 dimethoxy 96-41-3, Cyclopentanol 98-01-1, 2 Furancarboxaldehyde, reactions 98-80-6, Phenylboronic acid 98-86-2, Acetophenone, reactions 99-61-6 100-10-7 100-27-6 100-49-2, Cyclohexanemethanol 100-51-6, Benzyl alcohol, reactions 100-52-7, Benzaldehyde, reactions 101-98-4 104-20-1 104-53-0, 3 Phenylpropanal 105-13-5 108-01-0, 2 Dimethylaminoethanol 108-94-1, Cyclohexanone, reactions 110-85-0, Piperazine, reactions 111-27-3, 1 Hexanol, reactions 111-71-7, Heptanal 122-84-9 122-97-4, Benzenepropanol 122-99-6 123-51-3, 3 Methyl 1 butanol 346-06-5 349-75-7 349-95-1, Benzenemethanol 4 trifluoromethyl 387-45-1 401-95-6, Benzaldehyde 3 5 bis trifluoromethyl 437-81-0 440-60-8 447-61-0 455-01-6 455-19-6 456-47-3 459-56-3 459-57-4 492-88-6 495-76-1, 1,3-Benzodioxole-5-methanol 505-66-8, Homopiperazine 530-93-8, 2 Tetralone 536-60-7 552-89-6, 2 Nitrobenzaldehyde 555-16-8, reactions 587-03-1 589-18-4 589-92-4, 4 Methylcyclohexanone 612-16-8 613-69-4 619-73-8 620-23-5 621-87-4 622-40-2, 4 Morpholineethanol 624-95-3, 3 3 Dimethyl 1 butanol 642-31-9, 9 Anthracenecarboxaldehyde 645-45-4, Benzenepropanoyl chloride 699-02-5, 4 Methylphenethyl alcohol 699-12-7 702-23-8 705-76-0 712-97-0 767-05-5, Cyclopentanepropanol 768-35-4 768-59-2 773-99-9, 1 Naphthaleneethanol 835-78-9 836-43-1 872-85-5, 4 Pyridinecarboxaldehyde 873-75-6 873-76-7 874-42-0 939-97-9 947-91-1, Diphenylacetaldehyde 1122-72-1 1122-91-4 1124-63-6, Cyclohexanepropanol 1203-68-5, [1,1'-Biphenyl]-2-carboxaldehyde 1423-27-4 1466-74-6 1468-95-7, 9-Anthracenemethanol 1550-35-2 1586-00-1 1592-38-7, 2 Naphthalenemethanol 1620-98-0 1656-44-6, 2 4 Dinitrophenylsulfonyl chloride 1679-18-1 1700-30-7 1700-37-4 1765-93-1 1777-82-8, Benzenemethanol 2 4 dichloro 1805-32-9 1875-88-3 1971-81-9 1993-03-9 2043-61-0, Cyclohexanecarboxaldehyde 2192-55-4 2344-70-9 2426-87-1 2516-33-8, Cyclopropanemethanol 2646-90-4 2646-91-5 2928-43-0, [1,1'-Biphenyl]-2-methanol 3027-13-2 3040-44-6, 1 Piperidineethanol 3179-63-3, 3 Dimethylaminopropanol 3218-36-8, [1,1'-Biphenyl]-4-carboxaldehyde 3360-41-6, Benzenebutanol 3446-89-7 3446-90-0 3597-91-9, 4 Biphenylmethanol 3612-20-2 3637-61-4, Cyclopentanemethanol 3840-31-1 3900-89-8 3929-47-3 4181-05-9 4363-93-3, 4 Quinolinecarboxaldehyde 4397-53-9 4441-30-9, 4 Morpholinepropanol 4441-57-0, Cyclohexanebutanol 4748-78-1

4780-79-4, 1 Naphthalenemethanol 5020-41-7, 3 Methoxybenzeneethanol
5122-94-1, [1,1'-Biphenyl]-4 Boronic acid 5182-44-5 5392-12-1, 1
Naphthalenecarboxaldehyde, 2 methoxy 5402-55-1, 2 Thiopheneethanol
5406-18-8 5653-67-8 5720-05-8, 4 Methylbenzeneboronic acid 5720-06-9
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13512-59-9 13605-19-1 13669-42-6, 3 Quinolinecarboxaldehyde
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naphthalenyl 14615-72-6 15258-73-8 15341-08-9 15480-00-9
15852-73-0 15952-61-1 16152-51-5 16419-60-6 16588-34-4
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difluoro 19819-95-5 19819-98-8, 2 Methylphenethyl alcohol 20866-55-1
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30084-90-3, 9H-Fluorene-2-carboxaldehyde 30418-59-8 32316-92-0
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36880-33-8 39515-51-0 39742-60-4 40811-49-2 42454-06-8
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56456-47-4 56456-50-9 57260-71-6 59664-42-5 60211-57-6
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RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs.
as **melanocortin** agonists)

IT 73852-19-4 78725-46-9 79124-76-8 81028-92-4 81156-68-5
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91339-47-8 94464-94-5 94839-07-3 98437-23-1 98546-51-1
100124-06-9 107099-99-0 107572-07-6 108847-20-7 111033-77-3,
[1,1'-Biphenyl]-2-ethanol 122452-59-9 122775-35-3 123324-71-0
128796-39-4 130333-46-9 133730-34-4 139301-27-2, 4
Trifluoromethoxybenzeneboronic acid 144432-85-9 151169-74-3
151169-75-4 162976-08-1 163105-89-3 177259-98-2 182163-96-8,
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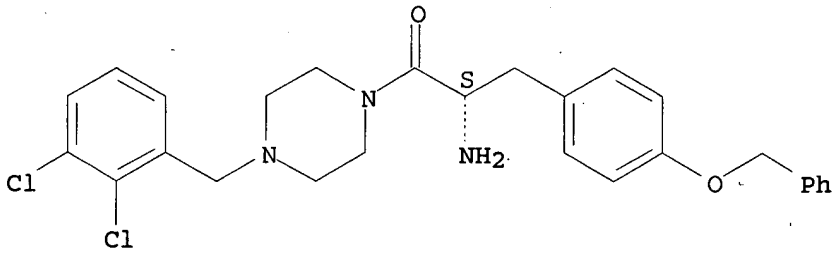
206551-43-1 216019-28-2 600729-18-8 636607-99-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs.
as **melanocortin** agonists)

IT 64263-81-6P **636607-94-8P 636607-95-9P**
636607-96-0P 636607-97-1P 636607-98-2P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**
(Preparation); RACT (Reactant or reagent)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs.
as **melanocortin** agonists)

IT **636605-31-7P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP**
(Preparation); THU (Therapeutic use); **PREP (Preparation)**;
PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of N-(α-aminoacyl)piperazine and -homopiperazine derivs.
as **melanocortin** agonists)

RN 636605-31-7 HCAPLUS
CN Piperazine, 1-[(2S)-2-amino-1-oxo-3-[4-(phenylmethoxy)phenyl]propyl]-4-
[(2,3-dichlorophenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:913002 HCAPLUS
DN 139:395952
TI Substituted piperazine derivatives as **melanocortin** receptor ligands, and their preparation, pharmaceutical compositions, and use
IN Pontillo, Joseph; Marinkovic, Dragan; Lanier, Marion C.; Tran Joe Ahn; Arellano, Melissa; Parker, Jessica; Nelson, Jodie; Chen, Chen; Chen, Caroline; Jiang, Wanglong; White, Nicole; Tucci, Fabio C.
PA Neurocrine Biosciences, Inc., USA
SO PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	US 2004053933	A1	20040318	US 2003-434803	20030509
	EP 1503761	A1	20050209	EP 2003-724540	20030509
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OS MARPAT 139:395952
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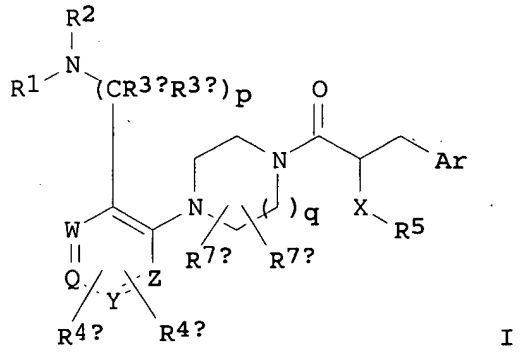

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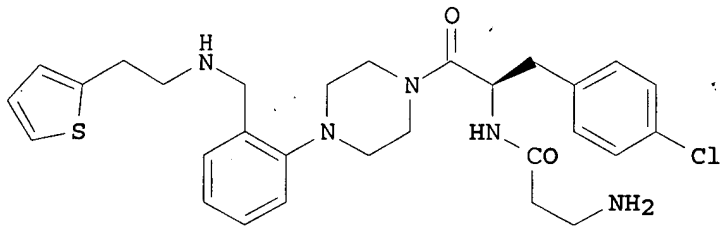

II

AB Compds. are disclosed, which function as **melanocortin** receptor ligands (no data), and which have utility in the treatment of **melanocortin**-receptor-based disorders. The compds. have structure I [q = 1 or 2; p = 1-3; W, Q, Y, Z = CH or N, provided that ≤ 2 are N, and that when 2 are N, then the N atoms are not adjacent; Ar = (un)substituted Ph or naphthyl; X = bond, O, S, N(R6a), N(R6a)C(O), N(R6a)S(O)2, N(R6a)C(O)N(R6b), C(O)O, OC(O), N(R6a)C(O)N(R6b)O, N(R6a)C(O)N(R6b)N(R6c), or N(R6a)C(O)O; R1, R2, R3a, R3b = H, (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl; R4a and R4b = optional ring substituents selected from OH, (un)substituted alkyl, cyano, halo, alkoxy, or alkylamino; R5 = H, (un)substituted alkyl, aryl, or heterocyclyl; R6a, R6b, R6c = H, (un)substituted alkyl; R7a, R7b = optional ring substituents selected from H and (un)substituted alkyl; provided that when p = 1 then R1, R2, R3a, and R3b cannot all be H; including stereoisomers, prodrugs, and pharmaceutically acceptable salts]. Pharmaceutical compns. containing I, as well as methods relating to their use, are also disclosed. Approx. 450 examples of compds. I and salts were prepared, as well as various intermediates. For instance, 1-Cbz-piperazine was N-arylated with 2-fluorobenzaldehyde (53%), followed by reductive amination of the aldehyde with 2-thiopheneethanamine, N-protection of the chain amino as the BOC derivative (82%, 2 steps), hydrogenolysis of CBZ (35%), peptide coupling with D-N-Fmoc-4-chlorophenylalanine using EDC, removal of Fmoc (87%, 2 steps), another peptide coupling with N-BOC-β-alanine, and removal of BOC, to give invention compound II, isolated as the trifluoroacetate salt.

IC ICM A61K031-496
ICS C07D333-20; C07D217-26; C07D295-18; C07D213-74; C07D211-52; C07D207-16; C07D207-32; C07D277-30; C07D307-16; C07D307-52; C07D207-34; C07D211-60; C07D211-62; C07D265-30; C07D233-02; C07D207-26; C07D317-58; C07D401-12; C07D403-12

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 2, 34

ST piperazine chlorophenylalanine peptidomimetic prepn **melanocortin** receptor ligand agonist antagonist

IT Peptides, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(analogs; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Sexual disorders
(impotence, treatment of; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 3; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor 4; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Hormone antagonists
Hormones, animal, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT Cachexia
Eating disorders
Sexual disorders
Skin, disease
(treatment of; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT 626212-33-7P 626217-48-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT 626208-21-7P 626208-22-8P 626208-23-9P 626208-24-0P 626208-25-1P
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626208-49-9P 626208-52-4P 626208-56-8P 626208-57-9P 626208-61-5P
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626208-97-7P 626209-00-5P 626209-02-7P 626209-05-0P 626209-08-3P
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626209-39-0P 626209-42-5P 626209-45-8P 626209-47-0P 626209-50-5P
626209-53-8P 626209-56-1P 626209-59-4P 626209-62-9P 626209-65-2P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

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627051-08-5P 627051-09-6P 627051-10-9P 627051-11-0P 627051-12-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT 55676-21-6P, 2-Chloro-3-acetylpyridine 128071-75-0P, 2-Bromo-3-formylpyridine 174855-57-3P 179556-15-1P 511539-64-3P
626218-86-8P 626218-91-5P 626218-95-9P 626218-99-3P 626219-03-2P
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626220-82-4P 626220-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

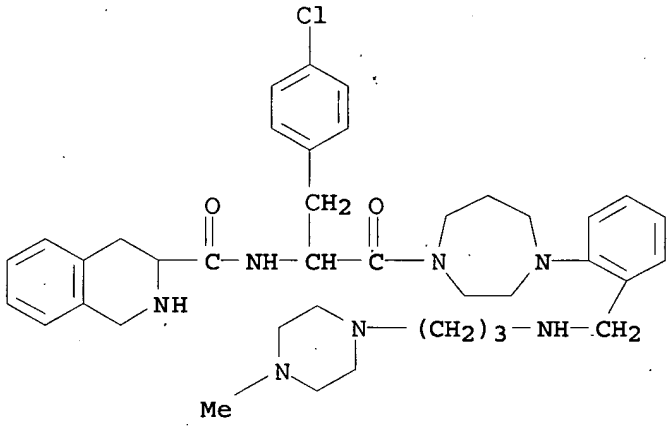
IT 75-31-0, Isopropylamine, reactions 89-99-6, 2-Fluorobenzylamine 96-15-1, 2-Methylbutylamine 103-55-9 109-04-6, 2-Bromopyridine 109-89-7, Diethylamine, reactions 110-85-0, Piperazine, reactions 394-47-8, 2-Fluorobenzonitrile 437-81-0, 2,6-Difluorobenzaldehyde 445-27-2, 2'-Fluoroacetophenone 446-52-6, 2-Fluorobenzaldehyde 920-36-5 926-62-5, Isobutyl magnesium bromide 927-58-2 1490-25-1, Methyl 4-chloro-4-oxobutyrate 1932-03-2, 1-(2-Chloroethyl)piperidine 1943-83-5, 2-Chloroethyl isocyanate 2045-79-6, 2-Methoxyphenethylamine 3303-84-2 4801-27-8, 2-Bromoethyl chloroformate 6602-54-6, 2-Chloro-3-cyanopyridine 30433-91-1, 2-Thiophen-2-ylethylamine 31166-44-6, Benzyl piperazine-1-carboxylate 38256-93-8, N-(2-Methoxyethyl)methylamine 52031-05-7 55144-92-8, 3-(2,4-Dichlorophenyl)propionic acid 57260-71-6, N-Boc-piperazine 57292-44-1 79710-86-4, Tetrahydrofuran-3-carboxaldehyde 89711-08-0, tert-Butyl N-(2-oxoethyl)carbamate 99636-38-1 112275-50-0 114872-98-9 114873-12-0 142994-19-2 146137-78-2, 2-Fluoro-5-trifluoromethylbenzaldehyde 146374-27-8 146514-35-4 151838-62-9 343338-28-3 626220-65-3 626220-70-0 626220-73-3

626220-76-6 626220-79-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

IT **626208-70-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of substituted piperazine derivs. as **melanocortin** receptor ligands)

RN 626208-70-6 HCAPLUS

CN 3-Isoquinolinecarboxamide, N-[1-[(4-chlorophenyl)methyl]-2-[hexahydro-4-[2-[[[3-(4-methyl-1-piperazinyl)propyl]amino]methyl]phenyl]-1H-1,4-diazepin-1-yl]-2-oxoethyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:656738 HCAPLUS
DN 139:197359
TI Preparation of pyrroles as ligands of **melanocortin** receptors
IN Dyck, Brian P.; Goodfellow, Val; Parker, Jessica; Phillips, Teresa; Wade, Warren; Tran, Joe Anh
PA Neurocrine Biosciences, Inc., USA
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003068738	A1	20030821	WO 2003-US4455	20030211

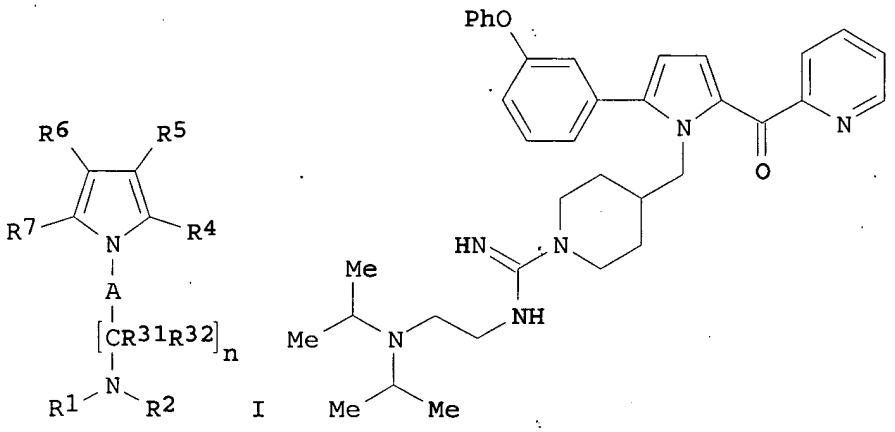
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2003216274	A1	20030904	AU 2003-216274	20030211
PRAI	US 2002-355867P	P	20020211		
	WO 2003-US4455	W	20030211		

OS MARPAT 139:197359

GI



AB The title compds. [I; A = a bond, NR8; n = 3-6; R1, R2 = H, alkyl, heterocyclyl, etc.; or NR1R2 = (un)substituted heterocyclyl; R31, R32 = H, alkyl, alkoxy, etc.; R4 = carbocyclyl, heterocyclyl, etc.; R5-R7 = H, halo, alkyl, etc.; R8 = H, alkyl, aryl, etc.] which function as **melanocortin** receptor ligands and having utility in the treatment of **melanocortin** receptor-based disorders (no data given), were prepared E.g., synthesis of II, was described. Table of 487 prepared compds. I was given. Pharmaceutical composition comprising the compound I was claimed.

IC ICM C07D207-32
ICS C07D401-04; C07D401-06; C07D401-12; C07D403-04; C07D403-12; C07D405-04; C07D405-14; C07D405-06; C07D409-04; C07D409-12; C07D413-12; C07D413-06; C07D417-12; C07D417-04; C07D521-00; A61K031-40; A61P017-00; A61P003-04

CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST pyrrole prepn **melanocortin** receptor agonist antagonist eating disorder skin

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of pyrroles as ligands of **melanocortin** receptors)

IT Appetite depressants
(preparation of pyrroles as ligands of **melanocortin** receptors)

IT Eating disorders
Skin, disease
(treatment of; preparation of pyrroles as ligands of **melanocortin** receptors)

IT 583845-50-5P 583845-51-6P 583845-52-7P 583845-53-8P 583845-54-9P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of pyrroles as ligands of **melanocortin** receptors)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrroles as ligands of **melanocortin** receptors)

IT 583850-20-8P 583850-21-9P 583850-22-0P 583850-23-1P 583850-24-2P
583850-25-3P 583850-26-4P 583850-27-5P 583850-28-6P 583850-29-7P
583850-30-0P 583850-31-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrroles as ligands of **melanocortin** receptors)

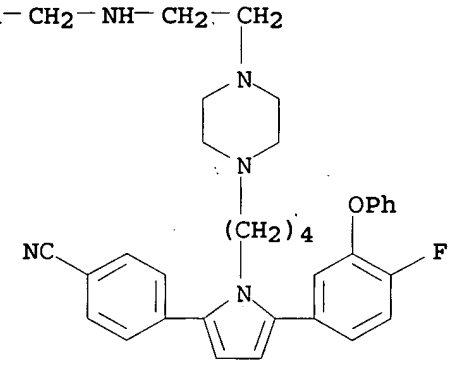
IT 121-05-1, 2-(Diisopropylamino)ethylamine 3034-53-5, 2-Bromothiazole
3586-12-7, 3-Phenoxyaniline 6457-49-4, 4-Piperidinemethanol 68766-96-1
111762-32-4, 3-Phenoxyphenylmagnesium bromide 583850-37-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrroles as ligands of **melanocortin** receptors)

IT 6876-00-2P 144978-35-8P 158407-04-6P 583850-32-2P 583850-33-3P
583850-34-4P 583850-35-5P 583850-36-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyrroles as ligands of **melanocortin** receptors)

IT **583847-04-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of pyrroles as ligands of **melanocortin** receptors)

RN 583847-04-5 HCAPLUS

CN Benzonitrile, 4-[5-(4-fluoro-3-phenoxyphenyl)-1-[4-[4-[2-[(phenylmethyl)amino]ethyl]-1-piperazinyl]butyl]-1H-pyrrol-2-yl]- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:511295 HCAPLUS
DN 139:85378
TI Preparation of piperazine derivatives as **melanocortin** 4 (MC4) receptor antagonists
IN Nakazato, Atsuro; Ishii, Takaaki; Nozawa, Dai
PA Taisho Pharmaceutical Co.,ltd., Japan
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003053927	A1	20030703	WO 2002-JP13317	20021219
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	CA 2470808	A1	20030703	CA 2002-2470808	20021219
	AU 2002357619	A1	20030709	AU 2002-357619	20021219
	EP 1468990	A1	20041020	EP 2002-805485	20021219
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	CN 1608050	A	20050420	CN 2002-825874	20021219
	US 2006084657	A1	20060420	US 2004-499011	20040618
	NO 2004003079	A	20040921	NO 2004-3079	20040720
PRAI	JP 2001-389419	A	20011221		
	WO 2002-JP13317	W	20021219		

OS MARPAT 139:85378
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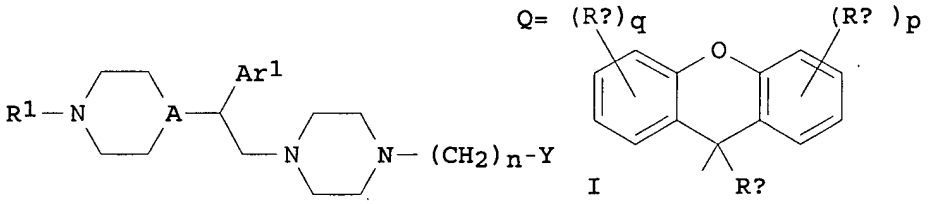

AB Piperazine derivs. represented by the formula (I) [wherein n = an integer of 1 to 8; R1 = H, C1-10 alkyl; A = CH, N; Ar1 = (un)substituted Ph; Y = a group represented by the formula Y1-Y2-Ar2 or Y3-Y4(Ar5)-Ar6; Y1-Y2 = a single bond, O, CO, CH:CH, N-C1-10 alkyl-(un)substituted CONH or NHCO; Ar2 = phthalimid-1-yl, dibenzofuranyl, C3-10 cycloalkyl, C2-9 oxacycloalkyl, C2-9 lactam-1-yl, 2,4-dioxo-1H-quinazolin-1-yl, etc.; Y3-Y4 = CH2C(Ra), CH:C, COCH; Ar5, Ar6 = (un)substituted Ph or Ar5 and Ar6 together with adjacent carbon atoms forms a group Q; wherein Ra = H, CO2H, C1-10 alkoxy-carbonyl, (un)substituted CONH2; Rd, Re = H, C1-10 alkyl, C1-10 alkoxy, aralkyloxy, HO, halo, NO2, NH2, mono- or di(C1-5 alkyl)amino, CF3, CF3O, cyano, CONH2; p, q = an integer of 1-3] or pharmaceutically acceptable salts thereof are prepared The novel piperazine derivs. has MC4 **melanocortin** receptor antagonistic activity and are useful for the treatment of anxiety neurosis or depression. Thus, 0.30 g 1-[2-(4-fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]piperazine was dissolved in 5 mL DMF, treated with 0.24 g 3-(biphenyl-2-yl)propionic acid, 0.21 g 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 0.18 g 1-hydroxybenzotriazole monohydrate, and 0.14 g Et3N, and stirred at room temperature overnight, after workup and silica gel chromatog., 0.34 g 1-[2-(4-fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[3-(biphenyl-2-yl)propionyl]piperazine which (0.30 g) was dissolved in 2.5 mL THF, treated with 21 mg LiAlH4, and refluxed for 30 min to give, after workup and silica gel chromatog., 0.19 g 1-[2-(4-fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[3-(biphenyl-2-yl)propyl]piperazine. 1-[2-(4-Fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[3-(2,4-diphenylthiazol-5-yl)propyl]piperazine inhibited the binding of [125I]Nle4-D-Phe7-α-MSH to HEK-293 cell membrane expressing human MC4 receptor with IC50 of 162 nM.

IC ICM C07D209-48
ICS C07D211-26; C07D231-12; C07D233-70; C07D233-84; C07D239-26; C07D239-42; C07D261-08; C07D263-32; C07D277-40; C07D277-56; C07D295-12; C07D295-14; C07D307-91; C07D313-18; A61K031-496; A61K031-517; A61P003-04; A61P025-22; A61P025-24

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST phenylpiperazinylethylbiphenylylpropylpiperazine prepn **melanocortin** 4 receptor antagonist; piperazine prepn **melanocortin** 4 receptor antagonist; phenylpiperazinylethylthiazolylpropylpiperazine prepn MC4 receptor antagonist; biphenylylpropylpiperazine prepn **melanocortin** 4 receptor antagonist; thiazolylpropylpiperazine prepn MC4 receptor antagonist; anxiety neurosis treatment piperazine prepn; depression treatment piperazine prepn

IT Mental and behavioral disorders
(depression; preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or

depression)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)
IT Mental and behavioral disorders
(neurosis, anxiety neurosis; preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)
IT Antidepressants
Anxiety
Anxiolytics
Human
(preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)
IT **552884-23-8P 552884-24-9P 552884-25-0P**
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552885-82-2P, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]-4-[3-(biphenyl-3-yl)propyl]piperazine **552885-85-5P**, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]-4-(4-cyclooctyl-4-oxobutyl)piperazine **552885-87-7P**, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]-4-[3-(4'-fluoro-1,1'-biphenyl-2-yl)-3-oxopropyl]piperazine **552885-89-9P**, 1-[2-(4-Fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[4,4-bis(4-fluorophenyl)-4-

carboxybutyl]piperazine **552885-90-2P**, 1-[2-(4-Fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[4,4-bis(4-fluorophenyl)-4-carbamoylbutyl]piperazine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)

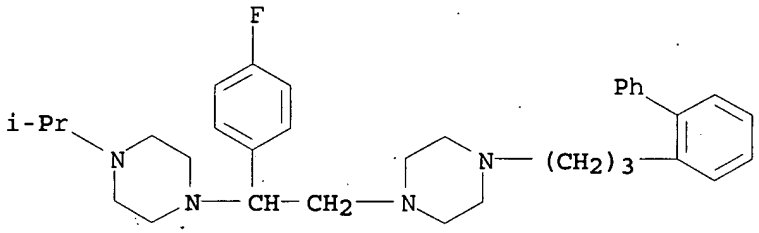
IT 62-56-6, Thiourea, reactions 75-30-9, 2-Iodopropane 120-43-4, 1-Ethoxycarbonylpiperazine 123-75-1, Pyrrolidine, reactions 405-50-5, p-Fluorophenylacetic acid 456-04-2, 2-Chloro-4'-fluoroacetophenone 4637-24-5 7803-57-8, Hydrazine monohydrate 19853-17-9, 3-(1,1'-Biphenyl-2-yl)propionic acid 24424-99-5, Di-tert-butyl dicarbonate 31166-44-6, 1-Benzyloxycarbonylpiperazine 79099-07-3, 1-tert-Butoxycarbonyl-4-piperidone 88569-66-8, 1-Isopropylpiperazine dihydrochloride 404362-38-5, 3-(Biphenyl-3-yl)propionic acid 552885-55-9, 2-(3-Bromo-2-propen-1-yl)biphenyl 552885-57-1, 2'-(3-Oxopropyl)-1,1'-biphenyl-4-carbonitrile 552885-75-3, 2-Acetyl-4'-fluorobiphenyl 552885-84-4, 4-Bromo-1-cyclooctylbutan-1-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)

IT 89011-45-0P, 1-Ethoxycarbonyl-4-[2-(4-fluorophenyl)-2-oxoethyl]piperazine 89011-47-2P, 1-Ethoxycarbonyl-4-[2-(4-fluorophenyl)-2-hydroxyethyl]piperazine hydrochloride 106000-09-3P, 1-Ethoxycarbonyl-4-[2-chloro-2-(4-fluorophenyl)ethyl]piperazine 385844-14-4P 385844-15-5P, 1-tert-Butoxycarbonyl-4-[carboxy(4-fluorophenyl)methyl]-3,6-dihydro-2H-pyridine 552885-52-6P, 1-Ethoxycarbonyl-4-[2-(4-fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]piperazine **552885-53-7P** **552885-54-8P** 552885-60-6P **552885-64-0P** **552885-65-1P** **552885-68-4P** **552885-71-9P** **552885-72-0P** 552885-74-2P 552885-77-5P, 1-tert-Butoxycarbonyl-4-[carboxy(4-fluorophenyl)methyl]piperidine **552885-78-6P**, 1-Benzyloxycarbonyl-4-[2-(1-tert-butoxycarbonylpiperidin-4-yl)-2-(4-fluorophenyl)acetyl]piperazine **552885-79-7P**, 1-Benzyloxycarbonyl-4-[2-(4-fluorophenyl)-2-(1-isopropylpiperidin-4-yl)acetyl]piperazine 552885-80-0P, 2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)-1-(piperazin-1-yl)ethanone **552885-81-1P**, 3-(Biphenyl-3-yl)-1-[4-[2-(4-fluorophenyl)-2-(1-isopropylpiperidin-4-yl)acetyl]piperazin-1-yl]propan-1-one 552885-83-3P, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]piperazine 552885-86-6P, 1-[2-(4-Fluorophenyl)-2-(1-isopropylpiperidin-4-yl)ethyl]piperazine trihydrochloride **552885-88-8P**, 1-[2-(4-Fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-[4,4-bis(4-fluorophenyl)-4-methoxycarbonylbutyl]piperazine **552885-91-3P**, 1-[2-(4-Fluorophenyl)-2-(4-isopropylpiperazin-1-yl)ethyl]-4-(4-ethoxycarbonyl-5-oxo-5-phenylpentyl)piperazine
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)

IT **552884-23-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine derivs. as **melanocortin** 4 (MC4) receptor antagonists for treatment of anxiety neurosis or depression)

RN 552884-23-8 HCAPLUS
CN Piperazine, 1-(3-[1,1'-biphenyl]-2-ylpropyl)-4-[2-(4-fluorophenyl)-2-[4-(1-methylethyl)-1-piperazinyl]ethyl]-, tetrahydrochloride (9CI) (CA INDEX

NAME)



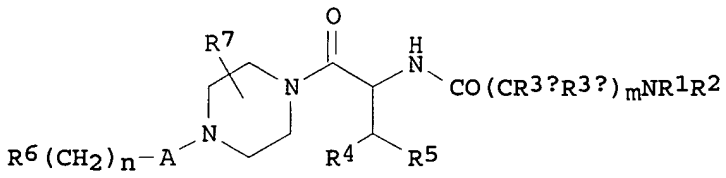
●4 HCl

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:301053 HCAPLUS
DN 138:321578
TI Preparation of peptides as ligands of **melanocortin** receptors
IN Dyck, Brian P.; Goodfellow, Val; Phillips, Teresa; Parker, Jessica; Zhang, Xiaohu; Chen, Chen; Tran, Joe Anh; Pontillo, Joseph; Tucci, Fabio C.
PA Neurocrine Biosciences, Inc., USA
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003031410	A1	20030417	WO 2002-US32282	20021009
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003158209	A1	20030821	US 2002-268923	20021009
	EP 1465867	A1	20041013	EP 2002-800985	20021009
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005506338	T	20050303	JP 2003-534394	20021009
PRAI	US 2001-328295P	P	20011009		
	US 2002-366745P	P	20020322		
	WO 2002-US32282	W	20021009		

OS MARPAT 138:321578
GI



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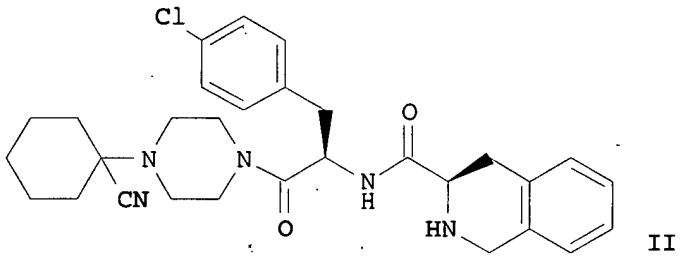

II

AB The invention relates to peptides I [m = 1-4; n = 0-4; A is (un)substituted alkanediyl; R1, R2, R3a, R3b = H, (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl or may combine to form rings; R1 or R2 may also be acyl; R4 = (un)substituted (hetero)aryl; R5 = H, OH, (un)substituted alkyl, aryl, or heterocyclyl; R6 = cyano, nitro, (un)substituted heterocyclyl, amino, carbamoyl, etc.; R7 = H or 1-4 substituents], or stereoisomers, prodrugs or pharmaceutically-acceptable salts, which function as **melanocortin** receptor ligands and may be used to treat disorders or illnesses including cachexia, obesity, diabetes, inflammation, and sexual dysfunction. Thus, treatment of cyclohexanone with sodium metabisulfite in H2O, followed by addition of Boc-protected piperazine and then NaCN, afforded 1-Boc-4-(1-cyanocyclohexyl)piperazine. The latter was converted into peptide II via coupling reaction.

IC ICM C07D209-42
ICS C07D209-44; C07D211-60; C07D213-38; C07D213-81; C07D213-82; C07D215-54; C07D217-26; C07D277-28; C07D295-18; C07D307-68; C07D333-20; C07D401-12; C07D487-08

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST peptide prepn ligand **melanocortin** receptor

IT Pain
(chronic; preparation of peptides as ligands of **melanocortin** receptors)

IT Sexual disorders
(impotence; preparation of peptides as ligands of **melanocortin** receptors)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of peptides as ligands of **melanocortin** receptors)

IT Antidepressants
Antiobesity agents
Anxiety
Anxiolytics
Cachexia
Eating disorders
Obesity

Sexual disorders
Skin, disease
(preparation of peptides as ligands of **melanocortin** receptors)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides as ligands of **melanocortin** receptors)

IT 511538-63-9P 511538-65-1P 511538-67-3P 511538-69-5P
511538-71-9P 511538-72-0P 511538-73-1P **511538-74-2P**
511538-75-3P **511538-76-4P** **511538-77-5P**
511538-78-6P **511538-79-7P** **511538-80-0P**
511538-81-1P **511538-82-2P** **511538-83-3P**
511538-84-4P 511539-03-0P 511539-04-1P 511539-05-2P
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511539-16-5P 511539-17-6P 511539-18-7P 511539-19-8P 511539-20-1P
511539-21-2P 511539-22-3P 511539-23-4P 511539-24-5P
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511549-53-4P 511549-54-5P 511549-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptides as ligands of **melanocortin** receptors)

IT 50-00-0, Formaldehyde, reactions 78-84-2, Isobutanal 98-03-3, 2-Thiophenecarboxaldehyde 98-80-6, Benzeneboronic acid 100-10-7 100-28-7, 4 Nitrophenyl isocyanate 100-52-7, Benzaldehyde, reactions 103-80-0, Phenylacetyl chloride 104-12-1, 4 Chlorophenyl isocyanate 104-53-0, 3 Phenylpropanal 105-07-7, 4 Cyanobenzaldehyde 108-94-1, Cyclohexanone, reactions 122-78-1, Phenylacetaldehyde 288-88-0, 1H-1,2,4-Triazole 298-12-4, Glyoxylic acid 446-52-6, Benzaldehyde, 2 fluoro 455-19-6 459-57-4 659-28-9 814-68-6, Acryloyl chloride 1003-29-8, 2 Pyrrolecarboxaldehyde 1121-60-4, 2-Pyridinecarboxaldehyde 1195-45-5, 4 Fluorophenyl isocyanate 1655-07-8, Ethyl 2 oxocyclohexanecarboxylate 1826-67-1, Vinylmagnesium bromide 2043-61-0, Cyclohexanecarboxaldehyde 2759-28-6, 1 Benzylpiperazine 2987-16-8, 3 3 Dimethylbutanal 4076-36-2, 5 Methyltetrazole 5416-93-3, 4 Methoxyphenyl isocyanate 10200-59-6, 2 Thiazolecarboxaldehyde 16227-06-8, N,N-Dimethylformamide azine dihydrochloride 16315-59-6, 4 Dimethylaminophenyl isocyanate 23138-53-6, 4 Methoxycarbonylphenyl isocyanate 24731-17-7, Ethyl 2 oxocyclohexaneacetate 31166-44-6

42036-65-7 52784-32-4, Methyl 2 oxocycloheptanecarboxylate 57260-71-6
57292-44-1 208645-11-8 252008-71-2 511539-64-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptides as ligands of **melanocortin** receptors)

IT 123892-38-6P 139754-93-1P 312272-32-5P 313492-86-3P 347186-49-6P
511538-85-5P 511538-86-6P 511538-87-7P 511538-89-9P 511538-90-2P
511538-92-4P 511538-93-5P 511538-94-6P 511538-95-7P 511538-96-8P
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511540-36-6P 511540-37-7P 511540-38-8P 511540-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides as ligands of **melanocortin** receptors)

IT 313276-51-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of peptides as ligands of **melanocortin** receptors)

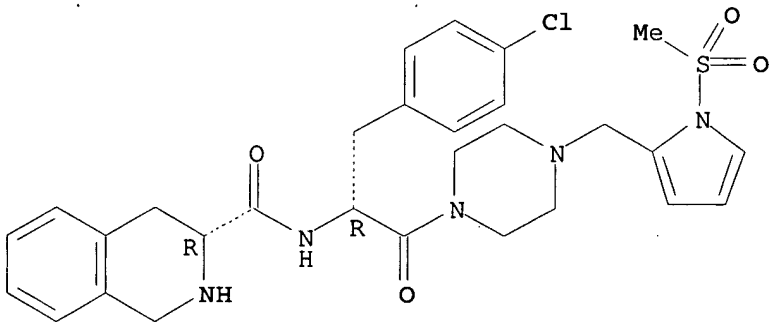
IT **511538-71-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptides as ligands of **melanocortin** receptors)

RN 511538-71-9 HCAPLUS
CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[[1-(methylsulfonyl)-1H-pyrrol-2-yl]methyl]-1-piperazinyl]-2-oxoethyl]-1,2,3,4-tetrahydro-, (3R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

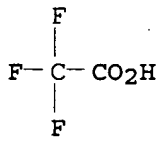
CRN 511538-70-8
CMF C29 H34 Cl N5 O4 S

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:133079 HCAPLUS
DN 138:188071
TI Peptidomimetics of biologically active metallopeptides
IN Sharma, Shubh D.; Shi, Yiqun; Rajpurohit, Ramesh; Wu, Zhijun
PA Palatin Technologies, Inc., USA
SO PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003013571	A1	20030220	WO 2002-US25574	20020812
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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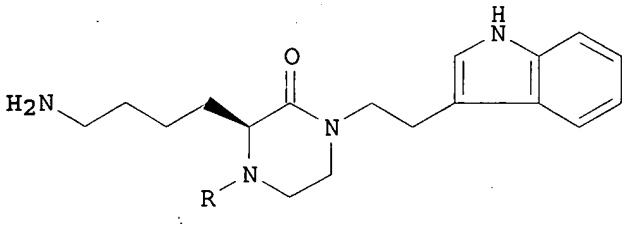
	US 2004157264	A1	20040812	US 2004-762079	20040121
	US 2004167201	A1	20040826	US 2004-776657	20040210
	US 2004171520	A1	20040902	US 2004-776419	20040210
	US 2005130988	A1	20050616	US 2005-36282	20050114
	US 2005124636	A1	20050609	US 2005-40838	20050121
	US 2005176728	A1	20050811	US 2005-99814	20050405
PRAI	US 2001-311404P	P	20010810		
	WO 2002-US25574	W	20020812		
	US 2003-467442P	P	20030501		
	US 2003-474497P	P	20030530		
	US 2004-536606P	P	20040114		
	US 2004-538100P	P	20040121		
	US 2004-761889	A2	20040121		
	US 2004-762079	A2	20040121		
	US 2004-546393P	P	20040219		
	US 2004-559741P	P	20040405		
	US 2004-563739P	P	20040419		
	US 2004-837519	A2	20040430		

OS MARPAT 138:188071

GI



I

AB The invention relates to a method of deriving a peptidomimetic of a biol. active metallopeptide. The peptidomimetic contains at least one non-peptide ring structure and at least two amino acid-related elements. The invention further relates to peptidomimetics with a template space heterocyclic ring structure, including 5-, 6- and 8-membered and 5-5 and 6-5 bicyclic fused ring structure **melanocortin** receptor-specific peptidomimetics. The examples describe the synthesis of pyrrolidines, 2-piperazinones [e.g., I [R = BuCH2CH2CO-Ser(Bzl)-D-Phe(2-Cl)]], hexahydropyrrolo[1,2-a]pyrazin-4-ones, hexahydropyrrolo[1,2-a]imidazol-3-ones, 1,4-benzodiazepines, and piperazines. Competitive inhibition testing of compound I against α-MSH yielded the following results at 1 μM: **melanocortin**-1 receptor (MC1-R) 96%, MC3-R 51%, MC4-R 99%, and MC5-R 82%.

IC ICM A61K038-00
ICS G01N031-00; G01N033-53; G06F019-00; C07K001-00; C07K014-00; C07D207-00; C07D209-02; C07D241-04; C07D295-00; C07D487-02

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7, 78

ST peptidomimetic prepn metallopeptide related inhibitor **melanocortin** receptor

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; peptidomimetics of biol. active metallopeptides)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(metallo-; peptidomimetics of biol. active metallopeptides)

IT Peptidomimetics
(peptidomimetics of biol. active metallopeptides)

IT **497935-98-5P 497935-99-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(peptidomimetics of biol. active metallopeptides)

IT 448944-52-3P **497934-80-2P 497934-81-3P**
497934-82-4P 497934-83-5P 497934-84-6P
497934-85-7P 497934-86-8P 497934-87-9P
497934-88-0P 497934-89-1P 497934-90-4P
497934-91-5P 497934-92-6P 497934-93-7P
497934-94-8P 497934-95-9P 497934-96-0P
497934-97-1P 497934-98-2P 497934-99-3P
497935-00-9P 497935-01-0P 497935-02-1P
497935-03-2P 497935-04-3P 497935-05-4P
497935-06-5P 497935-07-6P 497935-08-7P

497935-09-8P 497935-10-1P 497935-11-2P
497935-12-3P 497935-13-4P 497935-14-5P
497935-15-6P 497935-16-7P 497935-17-8P
497935-18-9P 497935-19-0P 497935-20-3P
497935-21-4P 497935-22-5P 497935-23-6P
497935-24-7P 497935-25-8P 497935-26-9P
497935-27-0P 497935-28-1P 497935-29-2P
497935-30-5P 497935-31-6P 497935-32-7P
497935-33-8P 497935-34-9P 497935-35-0P
497935-36-1P 497935-37-2P 497935-38-3P
497935-39-4P 497935-40-7P 497935-41-8P
497935-42-9P 497935-43-0P 497935-44-1P
497935-45-2P 497935-46-3P 497935-47-4P
497935-48-5P 497935-49-6P 497935-50-9P 497935-51-0P 497935-52-1P
497935-53-2P 497935-54-3P 497935-55-4P 497935-56-5P 497935-57-6P
497935-58-7P 497935-59-8P 497935-60-1P 497935-61-2P 497935-62-3P
497935-63-4P 497935-64-5P 497935-65-6P 497935-66-7P 497935-67-8P
497935-68-9P 497935-69-0P 497935-70-3P 497935-71-4P 497935-72-5P
497935-73-6P 497935-74-7P 497935-75-8P 497935-76-9P 497935-77-0P
497935-78-1P 497935-79-2P 497935-80-5P 497935-81-6P 497935-82-7P
497935-83-8P 497935-84-9P 497935-85-0P 497935-86-1P 497935-87-2P
497935-88-3P 497935-89-4P 497935-90-7P **497935-91-8P**
497935-92-9P 497935-93-0P 497935-94-1P
497935-95-2P 497936-96-3P 497935-97-4P
497936-00-2P 497936-01-3P 497936-02-4P 497936-03-5P 497936-04-6P
497936-05-7P 497936-06-8P 497936-07-9P 497936-08-0P 497936-09-1P
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497936-35-3P 497936-36-4P 497936-37-5P 497936-38-6P 497936-39-7P
497936-40-0P 497936-41-1P 497936-42-2P 497936-43-3P 497936-44-4P
497936-45-5P 497936-46-6P 497936-47-7P 497959-88-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(peptidomimetics of biol. active metallopeptides)

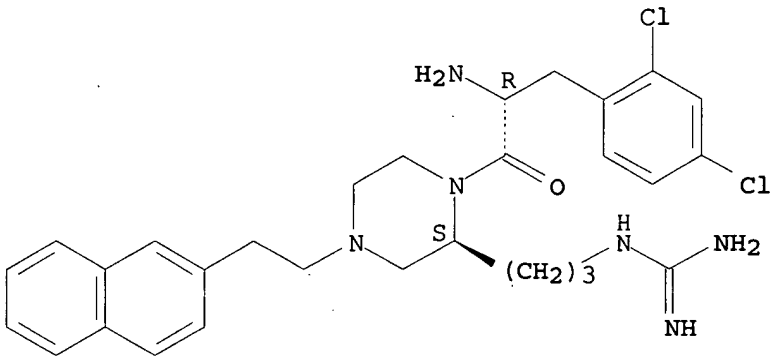
IT 2640-58-6 17442-18-1 22509-74-6 30924-93-7 107819-90-9, 1 3 Bis tert butoxycarbonyl 2 methyl 2 thiopseudourea 114873-12-0 245488-90-8 448902-19-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptidomimetics of biol. active metallopeptides)

IT 7767-00-2P 240436-46-8P 497934-77-7P 497934-78-8P 497934-79-9P
497936-48-8P 497936-49-9P 497936-50-2P **497936-51-3P**
497936-52-4P 497936-53-5P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(peptidomimetics of biol. active metallopeptides)

IT **497935-98-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(peptidomimetics of biol. active metallopeptides)

RN 497935-98-5 HCAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:97304 HCAPLUS
DN 138:137330
TI Preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes
IN Fotsch, Christopher H.; Arasasingham, Premilla; Bo, Yunxin; Chen, Ning; Goldberg, Martin H.; Han, Nianhe; Hsieh, Feng-Yin; Kelly, Michael G.; Liu, Qingyian; Norman, Mark H.; Smith, Duncan M.; Stec, Markian; Tamayo, Nuria; Xi, Ning; Xu, Shimin
PA Amgen Inc., USA
SO PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003009850	A1	20030206	WO 2002-US23926	20020725
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
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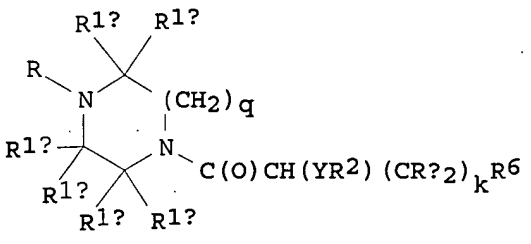
	US 2003220324	A1	20031127	US 2002-202823	20020724
	US 7115607	B2	20061003		
	CA 2454903	A1	20030206	CA 2002-2454903	20020725
	EP 1417190	A1	20040512	EP 2002-761189	20020725
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005503369	T	20050203	JP 2003-515242	20020725
PRAI	US 2001-307831P	P	20010725		
	US 2002-202823	A	20020724		
	WO 2002-US23926	W	20020725		

OS MARPAT 138:137330
GI



I

AB Selected substituted piperazine compds. (shown as I; variables defined below; e.g. (3S)-N-[(1S)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazinyl]-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide) are effective for prophylaxis and treatment of diseases, such as obesity and the like. The invention encompasses novel compds., analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compns. and methods for prophylaxis and treatment of diseases and other maladies or conditions involving activation of the **melanocortin** receptor. The subject invention also relates to processes for making such compds. as well as to intermediates useful in such processes. For I: Y is -NH-, -CH2-, or -O-; R = alkyl, -(CH2)n-cycloalkyl, -(CH2)n-aryl, and -(CH2)n-heterocyclyl; R1a, R1b, R1c, R1d, R1e, and R1f = R4; or R1a and R1b or R1d and R1c form oxo; or wherein R1e and R1c form an alkylenyl or alkenylenyl bridge; or R1a, R1b, R1c, R1d together with the piperazine ring forms an optionally substituted 1,2,3,4-tetrahydroquinoxalinyl ring. R2 = alkyl, -(CH2)n-cycloalkyl, -(CH2)n-aryl, -(CH2)n-heterocyclyl, -SO2R8, -C(O)R8; R4 = H, alkyl, -(CH2)n-cycloalkyl, -(CH2)n-aryl, -(CH2)n-heterocyclyl, halo, -(CH2)n-OR9, -NR9SO2R7, -[C(R7)2]pNR9SO2R7, -[C(R7)2]pNR9C(O)R7, -N(R9)2, -C(O)NR9R9, -NR9C(O)R7, -NR9CO2R7, cyano, -COOR9, -(CH2)n-C:OR7, -(CH2)n-C(S)R7, -(CH2)n-C(:NR9)R7, -NR9C(:NR7)N(R9)2, -[C(R7)2]pN(R9)2, nitro, -SO2N(R9)2, -S(O)mR7, -C(R7)2SO2CF3, hydroxyalkyl, haloalkyl and haloalkoxy. R6 = aryl and heteroaryl; Ra = H, and alkyl or the two Ra's together form cycloalkyl; k is 0 or 1; m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; p is 1 or 2; and q is 1 or 2; provisos and addnl. definitions are provided. In measurements of fast-induced food intake in mice, 6 examples of I caused a reduction in feeding at concns. ≤30 mg/kg. Although the methods of preparation are not claimed, 24 example prepns. of intermediates and >400 of I are included.

IC ICM A61K031-495
ICS C07D295-18; C07K005-078; C07K005-062; C07K005-065; C07D487-08; A61P003-04; A61K031-496; A61K031-55; C07D205-04; C07D211-60; C07D211-62; C07D317-68; C07D213-82; C07D213-81; C07D215-48; C07D213-38; C07D207-09; C07D209-14; C07D217-14

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 34

ST piperazine deriv prepn **melanocortin** receptor agonist antiobesity antidiabetic

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (agonists; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**melanocortin** receptor 4, agonists; preparation of substituted piperazines as agonists of **melanocortin** receptors useful

against obesity and diabetes)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor, agonists; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)
IT Antidiabetic agents
Antiobesity agents
Combinatorial library
Diabetes mellitus
Human
Obesity
(preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)
IT Drug delivery systems
(substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)
IT 494782-76-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-(morpholin-4-ylcarbonyl)phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-78-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(pyrrolidinocarbonyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-80-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-(N-methyl-N-benzylcarbamoyl)phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-82-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(N-prop-2-enylcarbamoyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-84-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(4-benzylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-86-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(4-methylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-88-6P, N-[2-[[2-[4-[(2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinol-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]phenyl]carbonylamino]ethyl]acetamide trifluoroacetate 494782-90-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-methyl-N-(2-phenylethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-92-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-(2-methylthioethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-94-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-[(4-chlorophenyl)methyl]carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-96-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(N-phenylcarbamoyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-98-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-[2-(1-methylpyrrolidin-2-yl)ethyl]carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-00-5P, N-[(1R)-2-[4-[2-[(4-Acetylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-02-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-[2-(3-phenoxyphenyl)ethyl]carbamoyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-04-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-(2-phenylethyl)carbamoyl]phenyl]pipe

razin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-06-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-(2-piperidylethyl)carbamoyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-08-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-(cyclohexylmethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3R)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494783-10-7P, N-[(1R)-2-[4-[2-[N-(2-Aminoethyl)carbamoyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 494782-29-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[[2-(methylamino)ethyl]amino]carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 494781-09-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3R)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide acetate 494781-10-1P, N-[(1R)-1-[(3,4-Dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494781-11-2P, N-[(1R)-1-[(3,4-Dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494781-19-0P, N-[(1R)-1-[(3,4-Dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]azetidine-3-carboxamide 494781-20-3P 494781-24-7P, N-[(1S)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494781-25-8P, (3S)-N-[(1S)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide acetate 494781-32-7P, N-[(1R)-1-[(4-Methoxyphenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494781-33-8P, N-[(1R)-1-[(4-Methoxyphenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494781-34-9P, N-[(1R)-2-[4-[2-[(Methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxo-1-[[4-(trifluoromethyl)phenyl]methyl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494781-35-0P, N-[(1R)-2-[4-[2-[(Methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxo-1-[[4-(trifluoromethyl)phenyl]methyl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494781-37-2P, N-[(1R)-2-[4-[2-[(Methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-(naphthylmethyl)-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494781-38-3P, N-[(1R)-2-[4-[2-[(Methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-(naphth-1-ylmethyl)-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494781-40-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-aminoacetamide 494781-41-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-aminoacetamide trifluoroacetate 494781-43-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]p

iperazin-1-yl]-2-oxoethyl]-(2S)-piperidine-2-carboxamide 494781-44-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2S)-piperidine-2-carboxamide trifluoroacetate 494781-47-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-aminopropanamide trifluoroacetate 494781-48-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-(methylamino)acetamide 494781-49-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-(methylamino)acetamide trifluoroacetate 494781-51-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2S)-2-amino-3-phenylpropanamide 494781-52-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2S)-2-amino-3-phenylpropanamide trifluoroacetate 494781-53-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]piperidine-4-carboxamide 494781-54-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]piperidine-4-carboxamide trifluoroacetate 494781-56-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2S)-2-amino-3-imidazol-4-ylpropanamide 494781-57-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2S)-2-amino-3-imidazol-4-ylpropanamide trifluoroacetate 494781-60-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-4-aminobutanamide trifluoroacetate 494781-62-3P, -N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2R)-azetidine-2-carboxamide 494781-63-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(2R)-azetidine-2-carboxamide trifluoroacetate 494781-65-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]indole-2-carboxamide 494781-67-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-methylindole-2-carboxamide 494781-69-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-chlorobenzamide 494781-72-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-4-chlorobenzamide 494781-75-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-methylbenzamide 494781-76-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-4-methoxybenzamide 494781-77-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-chlorobenzamide 494781-78-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3,4-dichlorobenzamide 494781-79-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-(trifluoromethyl)benzenecarboxamide 494781-80-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2H-benzo[d]-1,3-dioxolane-5-carboxamide 494781-81-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-4-(trifluoromethyl)benzamide 494781-82-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-phenylacetamide 494781-83-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]pyridine-3-carboxamide 494781-84-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]pyridine-2-carboxamide 494781-85-0P, N-[(1R)-1-[(4-

Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]pyridine-4-carboxamide 494781-86-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-methylpropanamide 494781-87-2P, N-[(R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]quinoline-6-carboxamide 494781-88-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]quinoline-6-carboxamide hemiacetate 494781-89-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]azetidine-3-carboxamide 494781-90-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]azetidine-3-carboxamide trifluoroacetate 494781-92-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[3-(aminomethyl)phenyl]carboxamide 494781-93-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-(aminomethyl)benzamide trifluoroacetate 494781-94-1P 494781-95-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]piperidine-3-carboxamide trifluoroacetate 494781-97-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-aminobenzamide trifluoroacetate 494781-98-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-methylpiperidine-2-carboxamide 494782-02-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-methylpiperidine-4-carboxamide 494782-03-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-(dimethylamino)propanamide 494782-04-6P, (2R)-3-(4-Chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-(benzylamino)propan-1-one monohydrochloride 494782-05-7P, (2R)-2-[[[4-(Dimethylamino)phenyl]methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one hydrochloride 494782-06-8P 494782-07-9P, (2R)-3-(4-Chlorophenyl)-2-[[(4-chlorophenyl)methyl]amino]-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one hydrochloride 494782-08-0P, (2R)-2-[[((2R)-Pyrrolidin-2-yl)methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494782-09-1P, (2R)-2-[[((2R)-Pyrrolidin-2-yl)methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one trifluoroacetate 494782-11-5P, (2R)-3-(4-Chlorophenyl)-2-[(indol-2-ylmethyl)amino]-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494782-12-6P, (2R)-3-(4-Chlorophenyl)-2-[(indol-2-ylmethyl)amino]-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one trifluoroacetate 494782-13-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-[(4-chlorophenyl)amino]propanamide 494782-14-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-[(4-chlorophenyl)amino]propanamide trifluoroacetate 494782-15-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-16-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-18-2P, (2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinolin-3-yl)methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494782-19-3P, (2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinol-3-yl)methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one trifluoroacetate 494782-20-6P, (2R)-2-[(2H,3H-Benzo[3,4-e]-1,4-

dioxin-6-ylmethyl)amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one monohydrochloride 494782-21-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[((2R)-pyrrolidin-2-yl)methoxy]carboxamide 494782-22-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[((2R)-pyrrolidin-2-yl)methoxy]carboxamide trifluoroacetate 494782-23-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(3-aminopropoxy)carboxamide 494782-24-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(3-aminopropoxy)carboxamide trifluoroacetate 494782-25-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[(3-aminopropyl)amino]carboxamide 494782-26-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[(3-aminopropyl)amino]carboxamide trifluoroacetate 494782-27-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[(4-piperidylmethyl)amino]carboxamide 494782-28-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[(4-piperidylmethyl)amino]carboxamide trifluoroacetate 494782-30-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-[[2-(methylamino)ethyl]amino]carboxamide trifluoroacetate 494782-31-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[methyl(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-32-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[methyl(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide mono(trifluoroacetate) 494782-35-3P, N-[(1R)-2-[4-[2-[(2-Aminoethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-36-4P, N-[(1R)-2-[4-[2-[(2-Aminoethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide bis(trifluoroacetate) 494782-39-7P, N-[(1S)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]azetidine-3-carboxamide 494782-43-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-44-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide bis(trifluoroacetate) 494782-46-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(2-methylpropyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-47-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(2-methylpropyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-48-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)(2-phenylethyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-49-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)(2-phenylethyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494782-50-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(propylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide hydrochloride 494782-51-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(2-thienylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-

tetrahydroisoquinoline-3-carboxamide hydrochloride 494782-52-4P, N-[2-[4-[(2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinol-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]phenyl]-2-methylpropanamide hydrochloride 494782-53-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[[[(2-nitrophenyl)methyl]sulfonyl]amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide hydrochloride 494782-54-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(3-pyridylcarbonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-55-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(3-pyridylcarbonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide monoacetate 494782-58-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-59-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide monoacetate 494782-61-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(phenylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide hemiacetate 494782-63-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(benzylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-64-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(benzylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide acetate 494782-66-0P
, N-[(1R)-2-[4-[2-[(2-Aminoethyl)amino]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-73-9P, N,N-Dimethyl-2-[4-[(2R)-2-[[((3S)-1,2,3,4-tetrahydroisoquinolin-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzamide 494782-74-0P, Methyl 2-[4-[(2R)-2-[[((3S)-1,2,3,4-tetrahydroisoquinol-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzoate 494782-75-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-(morpholin-4-ylcarbonyl)phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-77-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(pyrrolidinocarbonyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-79-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-(N-methyl-N-benzylcarbamoyl)phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-81-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(N-prop-2-enylcarbamoyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-83-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(4-benzylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-85-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(4-methylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-87-5P, N-[2-[[[2-[4-[(2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinolin-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]phenyl]carbonyl]amino]ethyl]acetamide 494782-89-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-methyl-N-(2-phenylethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-91-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-(2-methylthioethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-93-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-[(4-chlorophenyl)methyl]carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-95-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-(N-phenylcarbamoyl)phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-

tetrahydroisoquinoline-3-carboxamide 494782-97-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-[2-(1-methylpyrrolidin-2-yl)ethyl]carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494782-99-9P, N-[(1R)-2-[4-[2-[(4-Acetylpiperazin-1-yl)carbonyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-01-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-[2-(3-phenoxyphenyl)ethyl]carbamoyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-03-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-(2-phenylethyl)carbamoyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-05-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[N-(2-piperidylethyl)carbamoyl]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-09-4P, N-[(1R)-2-[4-[2-[N-(2-Aminoethyl)carbamoyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-11-8P, N-[(1R)-2-[4-[2-[(Dimethylamino)methyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-12-9P, N-[(1R)-2-[4-[2-[(Dimethylamino)methyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate (1:2.5) 494783-16-3P, N-[(1R)-2-[4-[2-[(Dimethylamino)methyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]azetidine-3-carboxamide 494783-17-4P 494783-20-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-(4-phenylpiperazin-1-yl)ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-23-2P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridyl)piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-24-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridyl)piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide monoacetate **494783-27-6P**, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridylmethyl)piperazin-1-yl]ethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-31-2P 494783-38-9P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]-1,4-diazepan-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-39-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]-1,4-diazepan-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide acetate 494783-44-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-(2-nitrophenyl)piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide hydrochloride 494783-45-8P, (2S)-3-(4-Chlorophenyl)-1-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-(phenylmethoxy)propan-1-one 494783-48-1P, (2S)-2-[(4-Chlorophenyl)methyl]-1-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-4-(1,2,3,4-tetrahydroisoquinol-2-yl)butane-1,4-dione 494783-56-1P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-[(cyclopropylmethyl)amino]ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-57-2P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [2-[4-[2-[1-(acetylmethylamino)ethyl]phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-58-3P, Quinoline-6-carboxylic acid [2-[4-[2-[1-[bis(cyclopropylmethyl)amino]ethyl]phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-59-4P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-(isobutylmethylamino)ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-60-7P, Quinoline-6-carboxylic acid [2-[4-[2-[[bis(cyclopropylmethyl)amino]methyl]phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-61-8P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[((cyclopropylmethyl)propylamino)methyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-62-9P, N-[1-(4-Chlorobenzyl)-2-[4-[2-[((cyclopropylmethyl)propylamino)methyl]-4-fluorophenyl]piperazin-1-

yl]-2-oxoethyl]-3-piperidin-1-ylpropionamide 494783-63-0P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-((methylsulfonylmethyl)amino)ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-64-1P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [2-[4-[2-[(2-aminoethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-65-2P 494783-66-3P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [2-[3-[(2-aminoethylcarbamoyl)methyl]-4-(2-methylsulfonylaminophenyl)piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-67-4P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [2-[4-[2-[1-[(4-acetylaminobenzyl)methylamino]ethyl]phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-68-5P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-[cyclopropylmethyl(3-methylbutyl)amino]ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-69-6P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-((cyclohexylmethyl)(cyclopropylmethyl)amino)ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-70-9P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-[cyclopropylmethyl(3-methylsulfanylpropyl)amino]ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-71-0P, 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid [2-[4-[4-bromo-2-(1-methylaminoethyl)phenyl]piperazin-1-yl]-1-(4-chlorobenzyl)-2-oxoethyl]amide 494783-72-1P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-[1-((cyclopropylmethyl)(thiophen-3-ylmethyl)amino)ethyl]phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-73-2P, Quinoline-6-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-74-3P, 1-Isobutylazetidine-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-75-4P, 1-(2,2-Dimethylpropyl)azetidine-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-76-5P, 1-(Cyclopropylmethyl)azetidine-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-77-6P, 4-Benzyloxy-N-[1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]benzamide 494783-78-7P, N-[1-(4-Chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]-3-methylaminopropionamide 494783-79-8P, N-[1-(4-Chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]-3,4-dimethoxybenzamide 494783-80-1P, Piperidine-4-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-((cyclopropylmethyl)(methylsulfonyl)amino)phenyl]piperazin-1-yl]-2-oxoethyl]amide 494783-81-2P, N-[(1R)-1-[(2-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-82-3P, N-[(1R)-1-[(3-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-83-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-3-aminopropanamide 494783-84-5P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-4-aminobutanamide 494783-85-6P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-2-aminobenzamide 494783-86-7P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(propylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-87-8P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-[2-[(2-thienylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-88-9P, N-[2-[4-[(2R)-2-[[((3S)-1,2,3,4-Tetrahydroisoquinolin-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]phenyl]-2-

methylpropanamide 494783-89-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[[[(2-nitrophenyl)methyl]sulfonyl]amino]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-90-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[N-(cyclohexylmethyl)carbamoyl]phenyl]piperazin-1-yl]-2-oxoethyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide 494783-91-4P, (2R)-3-(4-Chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-(benzylamino)propan-1-one 494783-92-5P, (2R)-2-[[[4-(Dimethylamino)phenyl]methyl]amino]-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494783-93-6P, (2R)-3-(4-Chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-[(2-pyridylmethyl)amino]propan-1-one 494783-94-7P, (2R)-3-(4-Chlorophenyl)-2-[[(4-chlorophenyl)methyl]amino]-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494783-95-8P **494789-84-3P**, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridylmethyl)piperazin-1-yl]ethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide trifluoroacetate 494789-85-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 494781-23-6P, tert-Butyl N-[[(1R)-1-[(3,4-dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]azetidine-3-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(drug candidate; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 494780-96-0P, 2-[4-[(2R)-2-[[((3S)-2-(tert-Butoxycarbonyl)-1,2,3,4-tetrahydroisoquinol-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzoic acid
RL: CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 59-67-6, Nicotinic acid, reactions 79-30-1, Isobutyryl chloride 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 92-54-6, 1-Phenylpiperazine 98-09-9, Benzenesulfonyl chloride 100-10-7, 4-Dimethylaminobenzaldehyde 100-39-0, Benzyl bromide 100-52-7, Benzaldehyde, reactions 103-63-9, (2-Bromoethyl)benzene 104-88-1, 4-Chlorobenzaldehyde, reactions 394-35-4, Methyl 2-fluorobenzoate 446-52-6, 2-Fluorobenzaldehyde 487-89-8, Indole-3-carboxaldehyde 501-52-0, 3-Phenylpropanoic acid 505-66-8, Homopiperazine 513-38-2, 1-Iodo-2-methylpropane 645-45-4, 3-Phenylpropanoyl chloride 1121-60-4, 2-Pyridinecarboxaldehyde 1493-27-2, 2-Fluoronitrobenzene 1939-99-7, α-Toluenesulfonyl chloride 2759-28-6, 1-Benzylpiperazine 3303-84-2, 3-tert-Butoxycarbonylaminopropionic acid 5292-43-3, tert-Butyl bromoacetate 7051-34-5, Cyclopropylmethyl bromide 10147-36-1, Propanesulfonyl chloride 10349-57-2, Quinoline-6-carboxylic acid 14091-08-8, p-Cl-D-Phe-OH 16629-19-9, 2-Thiophenesulfonyl chloride 21617-19-6, 3-(4-Chloroanilino)propionic acid 24974-75-2, 2-Nitro-α-toluenesulfonyl chloride 29668-44-8, 1,4-Benzodioxan-6-carboxaldehyde 57260-71-6 57292-44-1, N-Boc-p-Cl-D-Phe-OH 58885-58-8, N-(3-Hydroxypropyl)carbamic acid tert-butyl ester 59084-06-9, 1-(2-Nitrophenyl)piperazine 68090-88-0, N-Boc-4-chloro-L-phenylalanine 68790-38-5, 2-tert-Butoxycarbonylaminobenzoic acid 69610-41-9, N-Boc-L-prolinal 75178-96-0, tert-Butyl N-(3-aminopropyl)carbamate 78879-20-6, N-tert-Butoxycarbonyl-L-1,2,3,4-tetrahydroisoquinoline-3-

carboxylic acid 83435-58-9, N-Boc-D-prolinol 84358-12-3, Piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 84358-13-4, Piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 89711-08-0, tert-Butyl N-(2-oxoethyl)carbamate 98303-20-9, Piperidine-1,2-dicarboxylic acid 1-tert-butyl ester 102029-44-7, (4R)-4-(Phenylmethyl)-2-oxazolidinone 114873-13-1, N-Boc-D-3,4-dichlorophenylalanine 116258-17-4, (1S,4S)-2-Benzyl-2,5-diazabicyclo[2.2.1]heptane dihydrobromide 117445-22-4, 3-Boc-aminomethylbenzoic acid 121492-06-6, N-Boc-N-methylethylenediamine 130309-33-0, N-Fmoc-D-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid 142253-55-2 144222-22-0, 4-(Aminomethyl)-1-BOC-piperidine 147621-21-4, N-Boc-azetidine 343868-64-4, 1-(2-Piperidyl)piperazine 494780-73-3, (2R)-2-Amino-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494783-29-8, (2-Pyridylmethyl)piperazine 494783-52-7, (Cyclopropylmethyl)(methylsulfonyl)(2-piperazin-1-ylphenyl)amine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

IT 52085-96-8P, 3-(4-Chlorophenyl)propanoyl chloride 145525-27-5P, (3S)-N-Boc-1,2,3,4-tetrahydroisoquinoline-3-carboxaldehyde 159974-63-7P, Methyl 2-piperazin-1-ylbenzoate 170017-73-9P, tert-Butyl 4-(2-nitrophenyl)piperazine-1-carboxylate 170017-74-0P, tert-Butyl 4-(2-aminophenyl)piperazine-1-carboxylate 174855-57-3P, tert-Butyl 4-(2-formylphenyl)piperazine-1-carboxylate 199105-16-3P, 1-(2-Nitrophenyl)-4-benzylpiperazine 199105-17-4P, 2-(4-Benzylpiperazin-1-yl)phenylamine 199105-18-5P, (Methylsulfonyl)[2-(4-benzylpiperazin-1-yl)phenyl]amine 199105-23-2P, tert-Butyl 4-[2-[(dimethylamino)methyl]phenyl]piperazine-1-carboxylate 444582-15-4P, tert-Butyl 4-[2-[(methylsulfonyl)amino]phenyl]piperazine-1-carboxylate 444582-21-2P, tert-Butyl 4-[2-[methyl(methylsulfonyl)amino]phenyl]piperazine-1-carboxylate 444582-33-6P, tert-Butyl 4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazine-1-carboxylate 444583-44-2P, N-[(R)-1-[(4-Chlorophenyl)methyl]-2-[4-(2-nitrophenyl)piperazin-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 450352-64-4P, 1-(2-Nitrophenyl)-1,4-diazepan 494780-67-5P, (Methylsulfonyl)(2-piperazin-1-ylphenyl)amine hydrochloride 494780-69-7P, (2R)-[1-(4-Chlorobenzyl)-2-[4-(2-methylsulfonylaminophenyl)piperazin-1-yl]-2-oxoethyl]carbamic acid tert-butyl ester 494780-74-4P, (2R)-2-Amino-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one trifluoroacetate 494780-77-7P, (2R)-2-Amino-3-(4-chlorophenyl)-1-[4-(2-nitrophenyl)piperazin-1-yl]propan-1-one trifluoroacetate 494780-79-9P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-(2-nitrophenyl)piperazin-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494780-82-4P, tert-Butyl 3-[N-[(1R)-2-[4-(2-aminophenyl)piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494780-87-9P, Methyl 2-(4-benzylpiperazin-1-yl)benzoate 494780-90-4P, Methyl 2-[4-[(2R)-2-[[(tert-butoxy)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzoate 494780-92-6P, Methyl 2-[4-[(2R)-2-amino-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzoate hydrochloride 494780-94-8P, Methyl 2-[4-[(2R)-2-[[((3S)-2-(tert-butoxycarbonyl)-1,2,3,4-tetrahydroisoquinol-3-yl)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzoate 494780-99-3P, Fluoren-9-ylmethyl (3R)-3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-(2-nitrophenyl)piperazin-1-yl]-2-oxoethyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494781-04-3P, Fluoren-9-ylmethyl (3R)-3-[N-[(1R)-2-[4-(2-aminophenyl)piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline-

2-carboxylate 494781-06-5P, Fluoren-9-ylmethyl (3R)-3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494781-07-6P, (2R)-2-Amino-3-(4-chlorophenyl)-1-[4-(2-nitrophenyl)piperazin-1-yl]propan-1-one hydrochloride 494781-13-4P, N-[(1R)-1-[(3,4-Dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 494781-15-6P, (2R)-2-Amino-3-(3,4-dichlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494781-17-8P, tert-Butyl 3-[N-[(1R)-1-[(3,4-dichlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494781-26-9P, N-[(1S)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 494781-28-1P, (2S)-2-Amino-3-(4-chlorophenyl)-1-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494781-30-5P, tert-Butyl (3S)-3-[N-[(1S)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494781-91-8P, tert-Butyl N-[[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]azetidine-3-carboxylate 494781-99-6P, tert-Butyl 2-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]piperidine-1-carboxylate 494782-01-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]piperidine-2-carboxamide trifluoroacetate 494782-17-1P, [2-[4-[(2R)-2-Amino-3-(4-chlorophenyl)propyl]piperazin-1-yl]phenyl](methylsulfonyl)amine hydrochloride 494782-33-1P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[methyl(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 494782-34-2P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[methyl(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-37-5P, tert-Butyl 3-[N-[(1R)-2-[4-[2-[[2-[[(tert-butoxy)carbonyl]amino]ethyl]amino]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-38-6P, tert-Butyl 3-[N-[(1R)-2-[4-[2-[[2-[[(tert-butoxy)carbonyl]amino]ethyl](methylsulfonyl)amino]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-40-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 494782-41-1P, (2R)-2-Amino-3-(4-chlorophenyl)-1-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]propan-1-one 494782-42-2P, tert-Butyl N-[[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]azetidine-3-carboxylate 494782-45-5P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-56-8P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-[2-[(3-pyridylcarbonyl)amino]phenyl]piperazin-1-yl]ethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-57-9P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-62-6P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-[2-[(phenylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494782-65-9P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-[2-[(benzylsulfonyl)amino]phenyl]piperazin-1-yl]ethyl]carbamoyl]-(3S)-1,2,3,4-

tetrahydroisoquinoline-2-carboxylate 494782-67-1P, 2-(4-Benzylpiperazin-1-yl)benzoic acid 494782-68-2P, N,N-Dimethyl-2-(4-benzylpiperazin-1-yl)benzamide 494782-69-3P, N,N-Dimethyl-2-(piperazin-1-yl)benzamide 494782-70-6P, N,N-Dimethyl-2-[4-[(2R)-2-[[(tert-Butoxy)carbonyl]amino]-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzamide 494782-71-7P, N,N-Dimethyl-2-[4-[(2R)-2-Amino-3-(4-chlorophenyl)propanoyl]piperazin-1-yl]benzamide hydrochloride 494782-72-8P, tert-Butyl 3-[N-[(1R)-2-[4-[2-(N,N-dimethylcarbamoyl)phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-13-0P, Dimethyl[(2-piperazin-1-ylphenyl)methyl]amine 494783-14-1P, (2R)-2-Amino-1-[4-[2-[(dimethylamino)methyl]phenyl]piperazin-1-yl]-3-(4-chlorophenyl)propan-1-one 494783-15-2P, tert-Butyl 3-[N-[(1R)-2-[4-[2-[(dimethylamino)methyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-19-6P, tert-Butyl N-[[(1S)-2-[4-[2-[(dimethylamino)methyl]phenyl]piperazin-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]azetidine-3-carboxylate 494783-21-0P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-(4-phenylpiperazin-1-yl)ethyl]-1-(tert-butoxy)carboxamide 494783-22-1P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-(4-phenylpiperazin-1-yl)ethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-25-4P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridyl)piperazin-1-yl]ethyl]-1-(tert-butoxy)carboxamide 494783-26-5P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridyl)piperazin-1-yl]ethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate **494783-28-7P**, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridylmethyl)piperazin-1-yl]ethyl]-1-(tert-butoxy)carboxamide **494783-30-1P**, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridylmethyl)piperazin-1-yl]ethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-32-3P 494783-33-4P 494783-34-5P 494783-35-6P 494783-36-7P 494783-37-8P 494783-40-3P, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[4-(2-nitrophenyl)-1,4-diazepan-1-yl]-2-oxoethyl]-1-(tert-butoxy)carboxamide 494783-41-4P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-(2-nitrophenyl)-1,4-diazepan-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-42-5P, tert-Butyl 3-[N-[(1R)-2-[4-(2-aminophenyl)-1,4-diazepan-1-yl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-43-6P, tert-Butyl 3-[N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[(methylsulfonyl)amino]phenyl]-1,4-diazepan-1-yl]-2-oxoethyl]carbamoyl]-(3S)-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 494783-46-9P, N-(Cyclopropylmethyl)(methylsulfonyl)(2-piperazin-1-ylphenyl)amine 494783-47-0P, (2S)-3-(4-Chlorophenyl)-1-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-2-hydroxypropan-1-one 494783-49-2P, (4R)-3-[3-(4-Chlorophenyl)propanoyl]-4-benzyl-1,3-oxazolidin-2-one 494783-50-5P, tert-Butyl 4-((4R)-2-oxo-4-benzyl-1,3-oxazolidin-3-yl)-(3S)-3-[(4-chlorophenyl)methyl]-4-oxobutanoate 494783-51-6P, (2S)-3-[(tert-Butyl)oxycarbonyl]-2-[(4-chlorophenyl)methyl]propanoic acid 494783-53-8P, tert-Butyl (3S)-3-[(4-chlorophenyl)methyl]-4-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-4-oxobutanoate 494783-54-9P, (3S)-3-[(4-Chlorophenyl)methyl]-4-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-4-oxobutanoic acid **494783-55-0P**, tert-Butyl 4-[(3S)-3-[(4-chlorophenyl)methyl]-4-[4-[2-[(cyclopropylmethyl)(methylsulfonyl)amino]phenyl]piperazin-1-yl]-4-oxobutanoyl]piperazine-1-carboxylate 494796-54-2P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of substituted piperazines as agonists of **melanocortin**

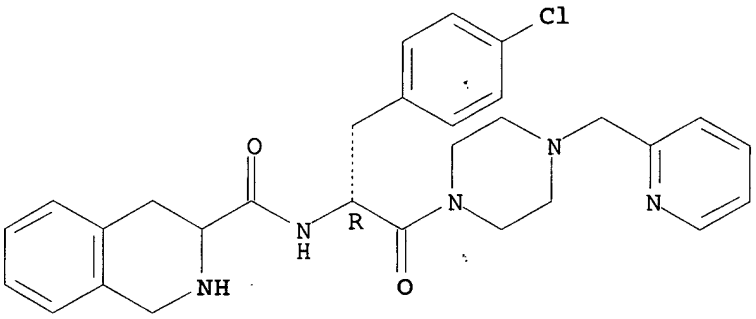
receptors useful against obesity and diabetes)

IT **494783-27-6P**, N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridylmethyl)piperazin-1-yl]ethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(drug candidate; preparation of substituted piperazines as agonists of **melanocortin** receptors useful against obesity and diabetes)

RN 494783-27-6 HCAPLUS

CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-oxo-2-[4-(2-pyridinylmethyl)-1-piperazinyl]ethyl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:898395 HCAPLUS

DN 138:100352

TI Structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding

AU Arasasingham, Premilla N.; Fotsch, Christopher; Ouyang, Xiaohu; Norman, Mark H.; Kelly, Michael G.; Stark, Kevin L.; Karbon, Bill; Hale, Clarence; Baumgartner, James W.; Zambrano, Martha; Cheetham, Janet; Tamayo, Nuria A.

CS Departments of Small Molecule Drug Discovery and Metabolic Disorders, Amgen Inc., Thousand Oaks, CA, 91320-1799, USA

SO Journal of Medicinal Chemistry (2003), 46(1), 9-11
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

OS CASREACT 138:100352

AB Agouti-related protein (AGRP) is an endogenous antagonist of the **melanocortin** action. In the hypothalamus, **melanocortin** peptide agonists act as satiety-inducing factors that mediate their action through the **melanocortin**-4 receptor (MC4R) whereas AGRP is an opposing orexigenic agent. Novel inhibitors of the AGRP/MC4 binding based on (piperazinylethyl)piperazines were prepared, and their structure-activity relationship was established.

CC 1-3 (Pharmacology)
Section cross-reference(s): 2, 27

ST arylpiperazinylethylpiperazine AGRP **melanocortin** 4 receptor antagonist structure satiety

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agouti-related; structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT Structure-activity relationship
(**melanocortin** 4 receptor binding; structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT Pituitary hormone receptors
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(**melanocortin** receptor 4, antagonists; structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT Appetite
(satiety; structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT Appetite depressants
Human
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT 60-92-4, Cyclic AMP
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT 110-85-0DP, Piperazine, arylpiperazinylethyl derivs. **89011-87-0P**
486439-01-4P 486439-03-6P 486439-04-7P
486439-22-9P 486439-23-0P 486439-24-1P
486439-25-2P 486439-26-3P 486439-27-4P
486439-28-5P 486439-29-6P 486439-30-9P
486439-31-0P 502623-66-7P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT 70-11-1 92-54-6 93-55-0 103-65-1 109-01-3 120-43-4, 1-Ethoxycarbonylpiperazine 121-97-1 403-29-2 529-34-0 536-38-9 711-33-1 3758-70-1 5308-25-8 6285-05-8 6582-42-9 17766-28-8 41011-01-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

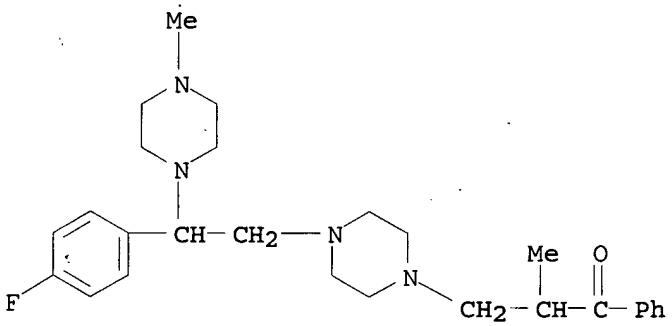
IT 89011-45-0P 89011-46-1P 89011-82-5P 106000-09-3P 189251-55-6P 344579-12-0P 486438-97-5P 486438-98-6P 486438-99-7P 486439-00-3P 486439-05-8P 486439-06-9P 486439-07-0P 486439-08-1P 486439-09-2P 486439-10-5P 486439-11-6P 486439-12-7P 486439-13-8P 486439-14-9P 486439-15-0P 486439-17-2P 486439-18-3P 486439-19-4P 486439-20-7P 486439-21-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

IT **89011-87-0P**

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(structure-activity relationship of (1-aryl-2-piperazinylethyl)piperazines: antagonists for the AGRP/**melanocortin** receptor binding)

RN 89011-87-0 HCAPLUS

CN 1-Propanone, 3-[4-[2-(4-fluorophenyl)-2-(4-methyl-1-piperazinyl)ethyl]-1-piperazinyl]-2-methyl-1-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:832817 HCAPLUS

DN 137:338139

TI Preparation of pyrrolidine, piperidine, or piperazine amino acid derivatives as **melanocortin** receptor ligands

IN Mazur, Adam Wieslaw; Tian, Xinrong; Hu, Xiufeng Eric; Ebetino, Frank Hallock

PA The Procter & Gamble Company, USA

SO PCT Int. Appl., 143 pp.
CODEN: PIXXD2

DT Patent

LA English

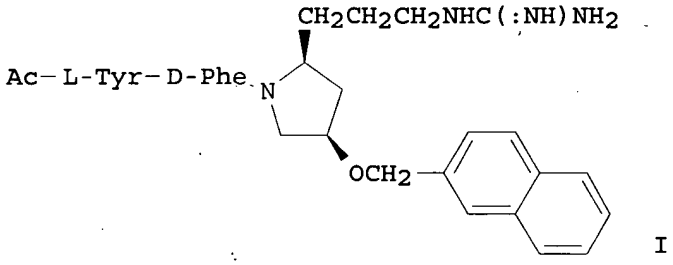
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002085925	A2	20021031	WO 2002-US13340	20020424
	WO 2002085925	A3	20031211		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003109556	A1	20030612	US 2002-121874	20020412
	US 6911447	B2	20050628		
	CA 2444599	A1	20021031	CA 2002-2444599	20020424
	EP 1390361	A2	20040225	EP 2002-723988	20020424
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	CN 1543461	A	20041103	CN 2002-808930	20020424

	JP 2005503342	T	20050203	JP 2002-583451	20020424
	BR 2002009193	A	20051025	BR 2002-9193	20020424
	RU 2277535	C2	20060610	RU 2003-134019	20020424
	ZA 2003007439	A	20041006	ZA 2003-7439	20030925
	NO 2003004774	A	20031229	NO 2003-4774	20031024
	US 2004224985	A1	20041111	US 2004-856983	20040528
	US 7087759	B2	20060808		
	US 2006106059	A1	20060518	US 2006-328330	20060109
PRAI	US 2001-286610P	P	20010425		
	US 2002-121874	A3	20020412		
	WO 2002-US13340	W	20020424		
	US 2004-856983	A1	20040528		

OS MARPAT 137:338139

GI



I

AB Disclosed are **melanocortin** (MC)-3/MC-4 receptor ligands of formula A(W)(Y)(Z), where A is a conformationally restricted ring, i.e., (non)aromatic carbocyclic or heterocyclic rings comprising 5-8 atoms, W is a unit which is preferably D-1-fluorophenyalanine, Y is pendant unit comprising at least one heteroatom, and Z is a pendant which comprises an aromatic carbocyclic ring. Also disclosed are pharmaceutical compns. comprising the ligands of the invention as well as methods of treating diseases mediated through MC-3/MC-4 receptors. Thus, compound I was prepared by a multistep procedure involving coupling reactions of 2(S)-(3-azidopropyl)-4(R)-(naphthalen-2-ylmethoxy)pyrrolidine, Boc-D-phenylalanine (Boc = tert-butoxycarbonyl), and N-acetyl-L-tyrosine.

IC ICM C07K

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 27, 28, 63

ST cyclic compd amino acid deriv **melanocortin** receptor ligand

IT Muscle, disease
(atrophy; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Shock (circulatory collapse)
(cardiogenic; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Artery, disease
(coronary; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Mental and behavioral disorders
(depression; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Gallbladder
(disease; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Body weight
(disorder; preparation of pyrrolidine, piperidine, or piperazine amino acid

derivs. as **melanocortin** receptor ligands)

IT Blood pressure
(elevated; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Embryo, animal
(fetus, intrauterine fetal growth; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Shock (circulatory collapse)
(hypovolemic; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Sexual disorders
(impotence; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Ovarian cycle
(irregularities; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor, ligands; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Diabetes mellitus
(non-insulin-dependent; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Anti-inflammatory agents
Antiarthritics
Antidepressants
Antihypertensives
Antitumor agents
Cardiovascular system, disease
Central nervous system
Fertility disorders
Gout
Hirsutism
Hypertension
Inflammation
Lung, disease
Memory disorders
Mental and behavioral disorders
Neoplasm
Osteoarthritis
Sepsis
Sexual disorders
Sleep apnea
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Dyslipidemia
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Amino acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Shock (circulatory collapse)
(septic; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT Embolism
(thromboembolism; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT 50-99-7, Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(intolerance; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT 474023-86-4P **474094-72-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

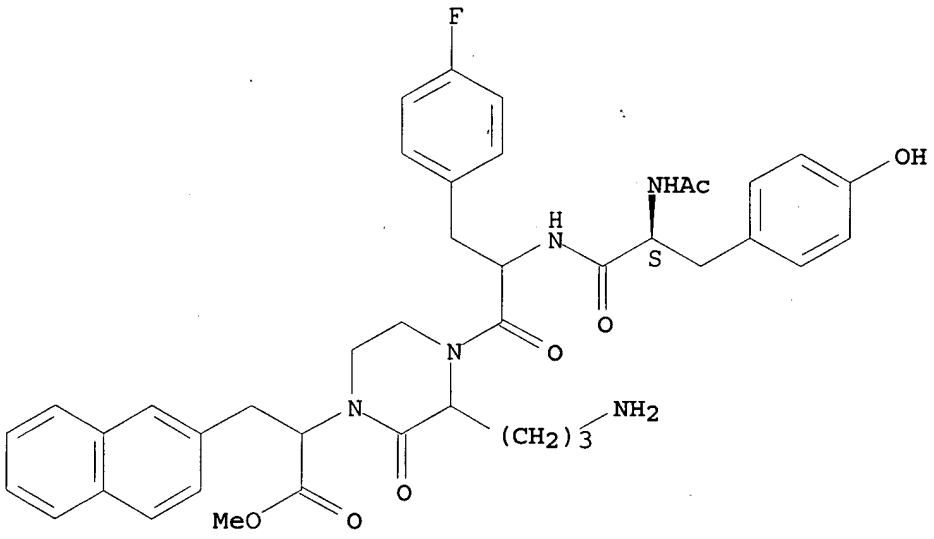
IT 474023-65-9P 474023-76-2P 474023-88-6P 474024-15-2P 474024-17-4P **474024-23-2P 474094-74-1P 474094-76-3P 474094-78-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT 64-04-0, Phenethylamine 79-04-9, Chloroacetyl chloride 106-93-4, 1 2 Dibromoethane 106-95-6, Allyl bromide, reactions 537-55-3, N-Acetyl-L-tyrosine 620-08-6, 4-Methoxypyridine 672-15-1, Homoserine 939-26-4, 2-(Bromomethyl)naphthalene 1694-92-4, o Nitrobenzenesulfonyl chloride 2017-68-7, 2 Naphthylethylamine 2480-93-5 2622-05-1, Allylmagnesium chloride 2799-21-5, r 3-Hydroxypyrrolidine 13726-85-7, N-tert-Butoxycarbonylglutamine 18942-49-9, N-(tert-Butoxycarbonyl)-D-phenylalanine 24974-75-2, 2-Nitrobenzylsulfonyl chloride 56583-58-5 57292-45-2 93983-56-3 107819-90-9, 1,3-Bis(tert-butoxycarbonyl)-2-methyl-2-thiopseudo urea 136282-47-8 151838-62-9 154476-57-0 264276-42-8 474024-24-3 **474024-25-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT 45172-42-7P 109431-87-0P 178549-93-4P 178549-94-5P 199006-28-5P 474023-54-6P 474023-55-7P 474023-56-8P 474023-57-9P 474023-58-0P 474023-59-1P 474023-60-4P 474023-61-5P 474023-62-6P 474023-63-7P 474023-64-8P 474023-66-0P 474023-67-1P 474023-68-2P 474023-69-3P 474023-70-6P 474023-71-7P 474023-72-8P 474023-73-9P 474023-74-0P 474023-75-1P 474023-77-3P 474023-78-4P 474023-79-5P 474023-80-8P 474023-82-0P 474023-83-1P 474023-84-2P 474023-85-3P 474023-87-5P 474023-89-7P 474023-90-0P 474023-91-1P 474023-92-2P 474023-93-3P **474023-94-4P 474023-95-5P 474023-96-6P** 474023-97-7P 474023-98-8P 474023-99-9P 474024-00-5P 474024-01-6P 474024-02-7P 474024-03-8P 474024-04-9P 474024-05-0P 474024-06-1P 474024-07-2P **474024-08-3P 474024-09-4P** 474024-10-7P 474024-11-8P 474024-12-9P 474024-13-0P 474024-14-1P 474024-16-3P 474024-18-5P **474024-19-6P 474024-20-9P 474024-21-0P 474024-22-1P 474094-71-8P 474094-73-0P 474094-75-2P 474094-77-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)

IT 108-98-5, Thiophenol, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance; preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)
IT **474094-72-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolidine, piperidine, or piperazine amino acid derivs. as **melanocortin** receptor ligands)
RN 474094-72-9 HCAPLUS
CN 1-Piperazineacetic acid, 4-(N-acetyl-L-tyrosyl-4-fluorophenylalanyl)-3-(3-aminopropyl)-α-(2-naphthalenylmethyl)-2-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L35 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:695975 HCAPLUS
DN 137:232913
TI Preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors
IN Yu, Guixue; Macor, John; Herpin, Timothy; Lawrence, R. Michael; Morton, George C.; Ruel, Rejean; Poindexter, Graham S.; Ruediger, Edward H.; Thibault, Carl
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

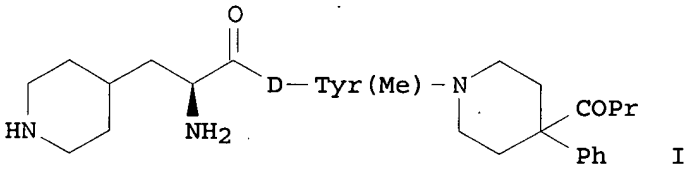
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002070511	A1	20020912	WO 2002-US6479	20020302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	CA 2437594	A1	20020912	CA 2002-2437594	20020302
	EP 1363898	A1	20031126	EP 2002-723310	20020302
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	HU 200401544	A2	20041228	HU 2004-1544	20020302
	JP 2005511475	T	20050428	JP 2002-569831	20020302
	US 2003092732	A1	20030515	US 2002-90582	20020304
	US 6979691	B2	20051227		
	US 2003096827	A1	20030522	US 2002-90288	20020304
	US 6713487	B2	20040330		
	US 2004229882	A1	20041118	US 2003-696761	20031029
	US 7067525	B2	20060627		
	US 2006025403	A1	20060202	US 2005-199464	20050808
PRAI	US 2001-273206P	P	20010302		
	US 2001-273291P	P	20010302		
	WO 2002-US6479	W	20020302		
	US 2002-90288	A3	20020304		
	US 2002-90582	A3	20020304		

OS MARPAT 137:232913

GI



I

AB Compds. W-(CR6R7)yCH(G)(CR4R5)xCO-X(R1)CHR2(CHR3)r(CH2)sCO-E [X = N or CH; R1, R3 = H or alkyl; R2 = H, aryl, cycloalkyl, heteroaryl, heterocyclyl, (un)substituted alkyl or alkenyl; R1 together with R2 or R3 or R2 together with R3 form mono- or bicyclic aryl, cycloalkyl, heteroaryl, or heterocyclyl; E = (un)substituted pyrrolidino, piperidino, hexahydro-1-azepinyl, 1-piperazinyl, cyclopentyl, cyclohexyl, cycloheptyl, amino, (cyclo)alkylamino; R4-R6 = H, (un)substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclyl; or CR4R5 or C6R7 is a spirocycloalkyl ring; r, s = 0 or 1; x = 0-4; y = 0-2; G = alkenyl, arylalkenyl, hydroxy, heteroaryl, cyano, functionalized alkyl or alkenyl, etc.; W = amino, alkylamino, hydroxy, alkoxy, carbamoyl, amidino, cycloalkyl, heteroaryl, heterocyclyl, etc.] were prepared as modulators of **melanocortin** receptors, particularly MC-1R and MC-4R. Thus, peptide I was prepared by a solution-phase peptide coupling/deprotection scheme.

IC ICM C07D401-00
ICS A61K031-445

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 2, 63

ST peptide prepn modulator **melanocortin** receptor

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT Peptides, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT Amino acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT 457893-83-3P 457893-85-5P 457893-95-7P 457893-96-8P 457893-98-0P
457893-99-1P 457894-21-2P 457894-26-7P 457894-27-8P 457894-28-9P
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457903-96-7P 457903-97-8P 457903-98-9P 457903-99-0P 457904-00-6P

457904-01-7P 457904-02-8P 457904-03-9P 457904-07-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT 457904-08-4P 457904-09-5P 457904-10-8P 457904-11-9P 457904-12-0P
457904-13-1P 457904-14-2P 457904-15-3P 457904-16-4P 457904-17-5P
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457904-23-3P 457904-24-4P 457904-25-5P 457904-26-6P 457904-27-7P
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457904-33-5P 457904-34-6P 457904-35-7P 457904-36-8P 457904-37-9P
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457904-44-8P 457904-45-9P 457904-46-0P 457904-47-1P 457904-48-2P
457904-49-3P 457904-50-6P 457904-51-7P 457904-52-8P 457904-53-9P
457904-54-0P 457904-55-1P 457904-57-3P 457904-59-5P 457904-60-8P
457904-61-9P **457904-62-0P** **457904-63-1P**
457904-64-2P **457904-65-3P** 457904-66-4P 457904-67-5P
457904-68-6P 457904-69-7P 457904-70-0P **457904-71-1P**
457904-72-2P 457904-73-3P 457904-74-4P 457904-75-5P
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457904-80-2P 457904-81-3P 457904-82-4P 457904-83-5P 457904-84-6P
457904-85-7P 457904-86-8P 457904-87-9P 457904-89-1P 459134-17-9P
459134-18-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

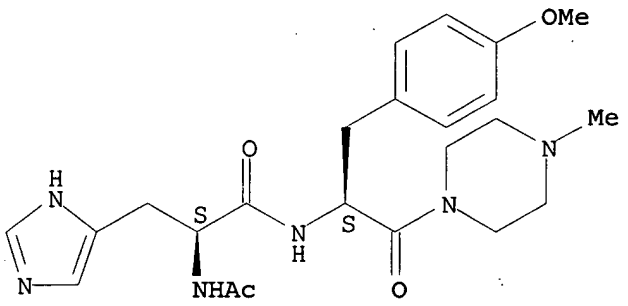
IT 79-22-1, Methyl chloroformate 98-09-9, Benzenesulfonyl chloride
109-61-5, Propyl chloroformate 124-63-0, Methanesulfonyl chloride
541-41-3, Ethyl chloroformate 594-44-5, Ethanesulfonyl chloride
1885-14-9, Phenyl chloroformate 1939-99-7, Phenylmethylsulfonyl chloride
10147-36-1, Propanesulfonyl chloride 15847-65-1 17791-52-5
68856-96-2 70601-64-8 204058-25-3 269726-94-5 312639-10-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT 457893-84-4P 457895-11-3P 457895-12-4P 457895-15-7P 457895-16-8P
457895-17-9P 457895-18-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

IT **457904-62-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptides for pharmaceutical use as modulators of **melanocortin** receptors)

RN 457904-62-0 HCAPLUS
CN 1H-Imidazole-4-propanamide, α-(acetylamino)-N-[(1S)-1-[(4-methoxyphenyl)methyl]-2-(4-methyl-1-piperazinyl)-2-oxoethyl]-, (αS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

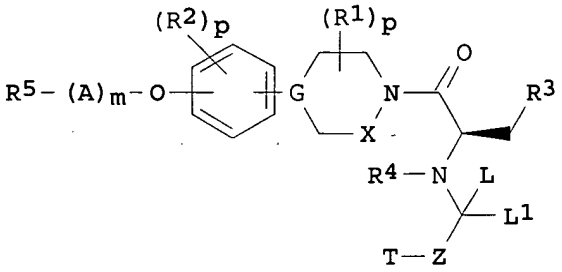


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:575075 HCAPLUS
DN 137:140779
TI Preparation of piperazine- and piperidine-derivatives as **melanocortin** receptor agonists
IN Briner, Karin; Doecke, Christopher William; Mancoso, Vincent; Martinelli, Michael John; Richardson, Timothy Ivo; Rothhaar, Roger Ryan; Shi, Qing; Xie, Chaoyu
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059117	A1	20020801	WO 2002-US515	20020123
	WO 2002059117	A8	20031106		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2432985	A1	20020801	CA 2002-2432985	20020123
	EP 1370558	A1	20031217	EP 2002-701922	20020123
	EP 1370558	B1	20050824		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004523530	T	20040805	JP 2002-559419	20020123
	AT 302773	T	20050915	AT 2002-701922	20020123
	ES 2246390	T3	20060216	ES 2002-2714719	20020123
	ES 2247298	T3	20060301	ES 2002-2701922	20020123
	US 2004082590	A1	20040429	US 2003-466248	20030711
PRAI	US 2001-263471P	P	20010123		
	WO 2002-US515	W	20020123		

OS MARPAT 137:140779
GI



I

AB The compds. of formula I [G = CR1, or N; A = alkyl, or cycloalkyl; L and L1 = H, or (together) oxo ; T = substituted indolyl, or pyrazinyl; X = CH2, or CH2CH2; Z = (CH2)n; R1 = H, alkyl, Ph, alkylaryl, alkylcarboxamide, cycloalkyl, or oxo; R2 = H, halo, alkyl, alkylsulfonyl, cycloalkyl, alkylaryl, or haloalkyl; R3 = (un)substituted aryl, or thienyl; R4 = H, alkyl, cycloalkyl, etc.; R5 = NH2, NPh2, alkylamide, alkylsulfonylamide, NHCOH, NHCONH2, NHSO2NH2, (un)substituted heterocyclyl, etc.; n = 0-8, m = 0-1, and p = 0-4], pharmaceutically acceptable salts, or stereoisomers were prepared as **melanocortin** receptor agonists for treatment of obesity, diabetes and male and/or female sexual dysfunction. Thus, coupling of 2-[(2-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinolin-3-ylmethyl)amino]-3-(4-chlorophenyl)propionate with 3-(2-piperazin-1-yltrifluoromethylphenoxy)-S-pyrrolidine-1-carboxylic acid tert-Bu ester, followed by deprotection and addition of HCl, gave 3-D-(4-chlorophenyl)-1-[4-[5-trifluoromethyl-2-S-(pyrrolidin-3-yloxy)phenyl]piperazin-1-yl]-2-D-[(1,2,3,4-tetrahydroisoquinoline-3-ylmethyl)amino]propan-1-one hydrochloride in 84% yield.

IC ICM C07D413-14
ICS C07D401-14; C07D401-12; C07D403-12; A61K031-495; A61K031-44

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28, 63

ST piperazine deriv peptidomimetic prepn **melanocortin** receptor agonist; piperidine deriv prepn antiobesity antidiabetic agent sexual dysfunction treatment; **melanocortin** receptor agonist peptide deriv prepn coupling

IT Peptides, preparation
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(derivs.; preparation of peptidomimetics as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT Sexual disorders
(impotence; preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT β3-Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with adrenoceptors agonists for treatment of obesity, diabetes and sexual dysfunction)

IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with sulfonylureas for treatment of obesity, diabetes and sexual dysfunction)

IT α2-Adrenoceptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with β3-adrenoceptor agonist for treatment of obesity, diabetes and sexual dysfunction)

IT Peptidomimetics
(preparation of peptidomimetics as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT Coupling reaction
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists by coupling)

IT Antidiabetic agents
Antiobesity agents
Diabetes mellitus
Human
Obesity
Sexual disorders
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT Amino acids, preparation
RL: CPS (Chemical process); PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 37250-24-1, HMG-CoA reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with HMG-CoA reductase inhibitor for treatment of obesity, diabetes and sexual dysfunction)

IT 82785-45-3, Neuropeptide Y
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with Neuropeptide Y antagonist for treatment of obesity, diabetes and sexual dysfunction)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with cholesterol lowering agent for treatment of obesity, diabetes and sexual dysfunction)

IT 9033-06-1, Glucosidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with glucosidase inhibitor for treatment of obesity, diabetes and sexual dysfunction)

IT 9004-10-8D, Insulin, mimetics 9004-10-8D, Insulin, sensitizers
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. of piperazine- and piperidine-derivs. with insulin for treatment of obesity, diabetes and sexual dysfunction)

IT 444583-61-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of)

IT 444605-11-2P
RL: BYP (Byproduct); PREP (Preparation)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 444584-20-7
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 444583-13-5P 444583-14-6P 444584-14-9P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 110-85-0DP, Piperazine, derivs. 110-89-4DP, Piperidine, derivs.
444604-00-6P 444604-01-7P 444604-02-8P 444604-03-9P 444604-04-0P
444604-05-1P 444604-06-2P 444604-07-3P 444604-08-4P 444604-09-5P
444604-10-8P 444604-11-9P 444604-12-0P 444604-13-1P 444604-14-2P
444604-15-3P 444604-16-4P 444604-17-5P 444604-18-6P 444604-19-7P
444604-20-0P 444604-21-1P **444604-22-2P** 444604-23-3P
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444604-34-6P 444604-35-7P 444604-36-8P 444604-37-9P 444604-38-0P
444604-39-1P 444604-40-4P 444604-41-5P 444604-42-6P 444604-43-7P
444604-44-8P 444604-45-9P 444604-46-0P 444604-47-1P 444604-48-2P
444604-49-3P 444604-50-6P 444604-51-7P 444604-52-8P 444604-53-9P
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444604-64-2P 444604-65-3P 444604-66-4P 444604-67-5P 444604-68-6P
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444604-89-1P 444604-90-4P 444604-91-5P 444604-92-6P 444604-93-7P
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444604-99-3P 444605-00-9P 444605-01-0P 444607-99-2P 444608-77-9P
444608-78-0P 444608-79-1P 444619-02-7P 444619-03-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 444584-18-3P 444584-21-8P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 79-03-8, Propionyl chloride 79-30-1, Isobutyryl chloride 85-44-9, 1,3-Isobenzofurandione 95-56-7, o-Bromophenol 98-09-9, Benzenesulfonyl chloride 98-88-4, Benzoyl chloride 100-46-9, Benzenemethanamine,

reactions 103-76-4, 2-Piperazin-1-yl-ethanol 108-16-7,
1-Dimethylamino-propan-2-ol 111-44-4 123-72-8, Butyraldehyde
124-63-0, Mesyl chloride 456-49-5, 3-Fluoroanisole 496-69-5,
2-Bromo-4-fluorophenol 594-44-5, Ethanesulfonyl chloride 622-40-2,
2-Morpholin-4-yl-ethanol 628-77-3 1072-85-1, 1-Bromo-2-fluorobenzene
1446-61-3, Dehydroabietylamine 2315-36-8, 2-Chloro-N,N-diethyl-acetamide
2605-67-6, Methyl(triphenyl phosphoranylidene)acetate 3647-69-6
3886-69-9 5382-16-1, 4-Hydroxypiperidine 5392-10-9 5465-63-4,
2-Bromobenzylamine hydrochloride 6630-33-7 6859-99-0, Piperidin-3-ol
7507-86-0 10147-37-2, Isopropylsulfonyl chloride 15028-44-1,
DL-Phenylalanine, methyl ester 18621-17-5 19432-27-0,
2-Bromo-4-isopropylphenol 21685-51-8, D-Phenylalanine, methyl ester
30135-88-7, Bromofluorobenzene 33965-47-8 53145-38-3 57292-45-2
61425-27-2 62291-95-6 69610-40-8 78879-20-6 79069-13-9
81107-97-3, 2-Bromo-4-trifluoromethyl phenol 82317-83-7 83435-58-9
84459-32-5 91599-81-4 94944-69-1 95798-22-4 103057-44-9
105400-81-5 106391-86-0 109384-19-2 109431-87-0 115962-35-1
120349-74-8 138647-49-1 140148-70-5 142994-19-2 198976-43-1
221352-46-1 313657-51-1 444583-76-0 444583-77-1 444606-54-6
444607-03-8 444607-12-9 444607-92-5 444608-06-4 444608-09-7
444608-12-2 444608-24-6 444608-27-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 96-33-3P 443-81-2P, 2-Bromo-3-fluorophenol 446-59-3P,
2-Bromo-3-fluoroanisole 2040-90-6P, 2-Chloro-6-fluorophenol 4045-27-6P
23123-19-5P 35532-01-5P 38574-55-9P 52753-91-0P 64282-11-7P
72388-13-7P 91640-73-2P 101558-72-9P 105226-66-2P 125213-45-8P
134166-72-6P 143900-43-0P 147067-88-7P 150220-29-4P 162356-90-3P
171662-92-3P 197971-07-6P 202187-17-5P 204926-10-3P 217462-09-4P
252008-71-2P 286961-14-6P 444583-12-4P 444583-15-7P 444583-18-0P
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444606-86-4P 444606-88-6P 444606-90-0P 444607-01-6P 444607-05-0P
444607-16-3P 444607-75-4P 444608-02-0P 444608-04-2P 444608-10-0P
444608-17-7P 444608-19-9P 444608-21-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT 6627-55-0P, 2-Bromo-4-methylphenol 252008-73-4P 444583-16-8P
444583-17-9P 444583-21-5P 444583-26-0P 444583-29-3P 444583-32-8P
444583-37-3P 444583-40-8P 444583-41-9P 444583-52-2P 444583-54-4P
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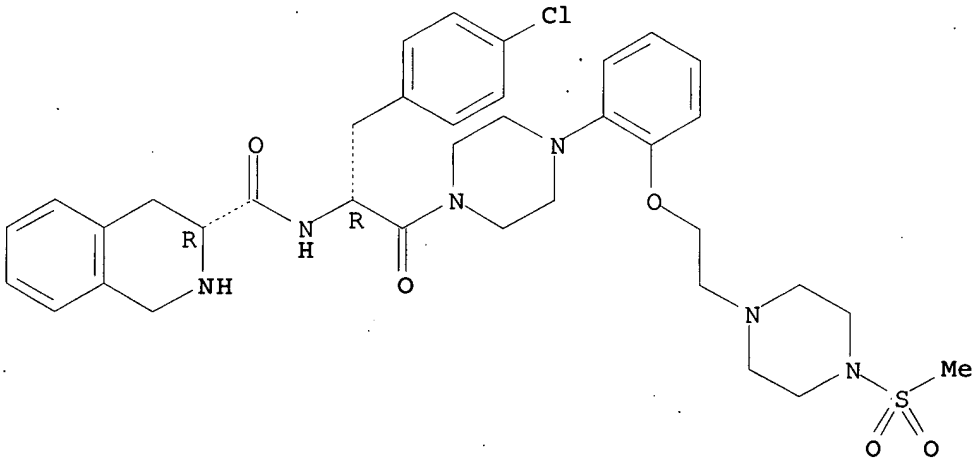
444607-07-2P 444607-10-7P 444607-14-1P 444607-18-5P 444608-80-4P
444619-04-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

IT **444604-22-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazine- and piperidine-derivs. as **melanocortin** receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

RN 444604-22-2 HCAPLUS
CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-[2-[2-[4-(methylsulfonyl)-1-piperazinyl]ethoxy]phenyl]-1-piperazinyl]-2-oxoethyl]-1,2,3,4-tetrahydro-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:575055 HCAPLUS
DN 137:140775
TI Preparation of piperazinyl and hexahydro-1,4-diazepinyl amino acid derivatives as **melanocortin** receptor agonists
IN Backer, Ryan Thomas; Briner, Karin; Collado Cano, Ivan; De Frutos-Garica, Oscar; Doecke, Christopher William; Fisher, Matthew Joseph; Garcia-Paredes, Cristina; Kuklish, Steven Lee; Mancoso, Vincent; Martinelli, Michael John; Mateo Herranz, Ana Isabel; Mullaney, Jeffrey Thomas; Ornstein, Paul Leslie; Wu, Zhipei; Xie, Chaoyu

PA Eli Lilly and Company, USA
SO PCT Int. Appl., 554 pp.
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LA English
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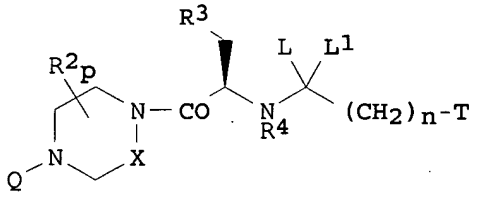
PI WO 2002059095	A1	20020801	WO 2002-US518	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432988	A1	20020801	CA 2002-2432988	20020123
EP 1358163	A1	20031105	EP 2002-701924	20020123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004524297	T	20040812	JP 2002-559397	20020123
US 2004116699	A1	20040617	US 2003-466250	20030711
PRAI US 2001-263380P	P	20010123		
WO 2002-US518	W	20020123		

OS CASREACT 137:140775; MARPAT 137:140775
GI



I

AB The invention relates to **melanocortin** receptor (MC-R) agonists I [X = CH2 or CH2CH2; LL1 = H2 or oxo; R2 = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cyclohexyl, or oxo if adjacent to N-Q; p = 0-4; R3 = (un)substituted Ph, aryl, or thienyl; R4 = H, alkyl, alkenyl, alkanoyl, or (D)phenyl; Q = various carbon-attached groups; T = isoquinolinyl or tetrahydro derivative, isoindolinyl, or piperazinyl; n = 0-8] which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperazinyl or hexahydro-1,4-diazepinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, N-[1-(4-chlorobenzyl)-2-[4-[1-(cyclohexylmethyl)-2-morpholinoethyl]piperazin-1-yl]-2-oxoethyl]-2-(2,3-dihydro-1H-isoindol-1-yl)acetamide tris(trifluoroacetate) salt was prepared via acylation of the piperazine moiety and showed EC50 = 69.3 nM in the MC-4 agonist assay.

IC ICM C07D217-26
ICS C07D217-04; C07D209-44; C07D417-12; A61K031-496; A61P003-00; A61P015-00; C07D217-12; C07K005-06
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28
ST piperazinyl hexahydrodiazepinyl amino acid prepn **melanocortin**

receptor agonist; diazepine hexahydro amino acid deriv prepn **melanocortin** receptor agonist; antiobesity piperazinyl hexahydrodiazepinyl amino acid prepn **melanocortin** receptor agonist; antidiabetic piperazinyl hexahydrodiazepinyl amino acid prepn **melanocortin** receptor agonist; sexual dysfunction treatment piperazinyl hexahydrodiazepinyl amino acid prepn

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor; preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT Antidiabetic agents
Antiobesity agents
Diabetes mellitus
Obesity
Sexual disorders
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT Amino acids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 444584-20-7
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 444584-15-0P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT **444892-36-8P 444892-72-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

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444893-29-2P 444893-41-8P 444894-64-8P
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444897-33-0DP, trifluoroacetic acid or hydrochloride salt
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trifluoroacetic acid or hydrochloride salt **444897-63-6DP**, trifluoroacetic acid or hydrochloride salt **444897-64-7DP**, trifluoroacetic acid or hydrochloride salt **444897-65-8DP**, trifluoroacetic acid or hydrochloride salt **444897-66-9DP**, trifluoroacetic acid or hydrochloride salt **444897-67-0DP**, trifluoroacetic acid or hydrochloride salt **444897-68-1DP**, trifluoroacetic acid or hydrochloride salt **444897-68-1P** **444897-69-2DP**, trifluoroacetic acid or hydrochloride salt **444897-69-2P** **444897-70-5DP**, trifluoroacetic acid or hydrochloride salt **444897-71-6DP**, trifluoroacetic acid or hydrochloride salt **444897-72-7DP**, trifluoroacetic acid or hydrochloride salt **444897-73-8DP**, trifluoroacetic acid or hydrochloride salt **444897-74-9DP**, trifluoroacetic acid or hydrochloride salt **444897-74-9P** **444897-75-0DP**, trifluoroacetic acid or hydrochloride salt **444897-76-1DP**, trifluoroacetic acid or hydrochloride salt **444897-77-2DP**, trifluoroacetic acid or hydrochloride salt **444897-78-3DP**, trifluoroacetic acid or hydrochloride salt **444897-79-4DP**, trifluoroacetic acid or hydrochloride salt **444897-80-7DP**, trifluoroacetic acid or hydrochloride salt **444897-81-8DP**, trifluoroacetic acid or hydrochloride salt **444897-81-8P** **444897-82-9DP**, trifluoroacetic acid or hydrochloride salt **444897-83-0DP**, trifluoroacetic acid or hydrochloride salt **444897-84-1DP**, trifluoroacetic acid or hydrochloride salt **444897-85-2DP**, trifluoroacetic acid or hydrochloride salt **444897-86-3DP**, trifluoroacetic acid or hydrochloride salt **444897-87-4DP**, trifluoroacetic acid or hydrochloride salt **444897-88-5DP**, trifluoroacetic acid or hydrochloride salt **444897-89-6DP**, trifluoroacetic acid or hydrochloride salt **444897-90-9DP**, trifluoroacetic acid or hydrochloride salt **444897-91-0DP**, trifluoroacetic acid or hydrochloride salt **444897-92-1DP**, trifluoroacetic acid or hydrochloride salt **444897-95-4DP**, trifluoroacetic acid or hydrochloride salt **444897-95-4P** **444897-96-5DP**, trifluoroacetic acid or hydrochloride salt **444897-97-6DP**, trifluoroacetic acid or hydrochloride salt **444897-98-7DP**, trifluoroacetic acid or hydrochloride salt **444897-99-8DP**, trifluoroacetic acid or hydrochloride salt **444898-00-4DP**, trifluoroacetic acid or hydrochloride salt **444898-01-5DP**, trifluoroacetic acid or hydrochloride salt **444898-02-6DP**, trifluoroacetic acid or hydrochloride salt **444898-03-7DP**, trifluoroacetic acid or hydrochloride salt **444898-04-8DP**, trifluoroacetic acid or hydrochloride salt **444898-05-9DP**, trifluoroacetic acid or hydrochloride salt **444898-06-0DP**, trifluoroacetic acid or hydrochloride salt **444898-07-1DP**, trifluoroacetic acid or hydrochloride salt **444898-08-2DP**, trifluoroacetic acid or hydrochloride salt **444898-09-3DP**, trifluoroacetic acid or hydrochloride salt **444898-10-6DP**, trifluoroacetic acid or hydrochloride salt **444898-11-7DP**, trifluoroacetic acid or hydrochloride salt **444898-12-8DP**, trifluoroacetic acid or hydrochloride salt **444898-13-9DP**, trifluoroacetic acid or hydrochloride salt **444898-14-0DP**, trifluoroacetic acid or hydrochloride salt **444898-15-1DP**, trifluoroacetic acid or hydrochloride salt **444898-16-2DP**, trifluoroacetic acid or hydrochloride salt

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT **444898-17-3DP**, trifluoroacetic acid or hydrochloride salt **444898-17-3P 444898-18-4DP**, trifluoroacetic acid or hydrochloride salt **444898-19-5DP**, trifluoroacetic acid or hydrochloride salt 444898-20-8DP, trifluoroacetic acid or hydrochloride salt **444898-21-9DP**, trifluoroacetic acid or hydrochloride salt **444898-22-0DP**, trifluoroacetic acid or hydrochloride salt 444898-23-1DP, trifluoroacetic acid or hydrochloride salt 444898-24-2DP, trifluoroacetic acid or hydrochloride salt **444898-25-3P 444898-26-4P 444898-27-5P 444898-28-6P 444904-66-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 444583-55-5P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 74-96-4, Ethyl bromide 75-07-0, Acetaldehyde, reactions 79-30-1, Isobutyryl chloride 85-41-6, Phthalimide 85-44-9, Phthalic anhydride 89-98-5, 2 Chlorobenzaldehyde 96-33-3, Methyl acrylate 100-52-7, Benzaldehyde, reactions 104-47-2 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 123-19-3, 4-Heptanone 123-75-1, Pyrrolidine, reactions 140-53-4, 4 Chlorobenzyl cyanide 437-81-0, 2,6 Difluorobenzaldehyde 446-52-6, 2 Fluorobenzaldehyde 447-61-0, o Trifluoromethyl benzaldehyde 615-83-8, Ethyl 2 bromovalerate 623-70-1 627-00-9, 4-Chlorobutyric acid 926-62-5, Isobutylmagnesium bromide 1132-26-9 1493-13-6, Trifluoromethanesulfonic acid 1529-41-5, 3 Chlorobenzyl cyanide 1550-35-2, 3,5 Difluorobenzaldehyde 1633-82-5 2043-61-0, Cyclohexanecarboxaldehyde 2338-75-2 2338-76-3 2605-67-6, Methyl triphenylphosphoranylidene acetate 2739-98-2 2856-63-5, 2 Chlorobenzyl cyanide 2942-58-7, Diethyl cyanophosphonate 2947-60-6, m Methylbenzyl cyanide 2947-61-7 3814-34-4, 1-Bromo 2 ethylbutane 3886-69-9 5292-21-7, Cyclohexylacetic acid 5392-10-9, 2-Bromo 4 5 dimethoxy benzaldehyde 5465-63-4, 2-Bromobenzylamine hydrochloride 5664-21-1, Cyclohexaneacetaldehyde 6624-49-3, 3-Isoquinolinecarboxylic acid 6630-33-7, 2-Bromobenzaldehyde 7035-03-2 7507-86-0, 2-Bromo 5 methoxy benzaldehyde 7677-24-9, Trimethylsilyl cyanide 14352-61-5 20989-17-7, s Phenylglycinol 33965-47-8 35166-78-0, Cyclohexylmethylmagnesium bromide 50598-92-0 56613-80-0, r Phenylglycinol 57260-71-6 57292-44-1 57292-45-2 57486-67-6 84459-32-5, 2-Bromo 5 nitrobenzaldehyde 89763-93-9, 3 Fluoro 5 Trifluoromethylbenzaldehyde 95299-17-5 105400-81-5 112275-50-0 114873-11-9 115962-35-1 150220-29-4 444583-77-1 444893-82-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 123-56-8P, Succinimide 2412-80-8P, Methyl 4-methylvalerate 3196-22-3P 4401-20-1P, Cycloheptaneacetic acid 24470-78-8P, Isopropyltriphenylphosphonium iodide 35532-01-5P 52753-91-0P 53731-99-0P 58327-36-9P 58851-63-1P 61837-46-5P 74376-32-2P 90775-10-3P 90775-12-5P 90775-14-7P 90775-15-8P 91640-73-2P 96788-17-9P 125213-45-8P 135357-91-4P 135660-93-4P 147067-88-7P 162356-90-3P 171662-92-3P 197971-07-6P 197972-23-9P 217462-09-4P 252008-71-2P 347186-49-6P 444583-12-4P 444583-13-5P 444583-14-6P 444583-15-7P 444583-16-8P 444583-17-9P 444583-18-0P 444583-19-1P 444583-20-4P 444583-21-5P 444583-22-6P 444583-23-7P 444583-24-8P 444583-25-9P 444583-26-0P 444583-29-3P 444583-40-8P 444583-48-6P

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RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT 444893-63-4P 444893-64-5P 444893-65-6P 444893-66-7P 444893-67-8P
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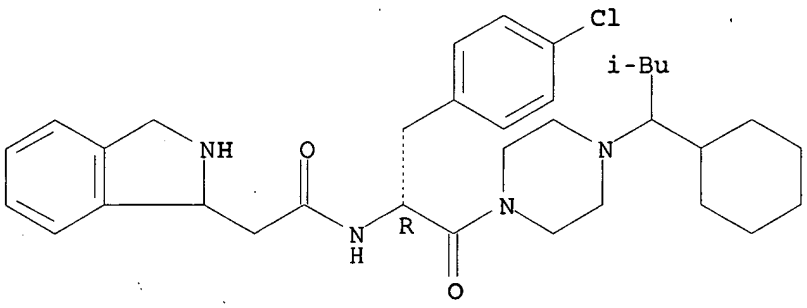
444896-78-0P 444896-79-1P 444896-80-4P
444896-81-5P 444896-82-6P 444897-27-2P
444897-28-3P 444897-29-4P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

IT **444892-36-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); **PREP (Preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as **melanocortin** receptor agonists)

RN 444892-36-8 HCAPLUS

CN 1H-Isoindole-1-acetamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[4-(1-cyclohexyl-3-methylbutyl)-1-piperazinyl]-2-oxoethyl]-2,3-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



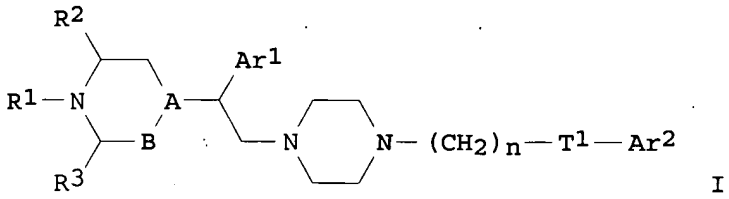
●2 HCl

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:10310 HCAPLUS
DN 136:79788
TI Remedial agent for anxiety neurosis or depression and piperazine derivative
IN Nakazato, Atsuro; Chaki, Shigeyuki; Okubo, Taketoshi; Ogawa, Shin-ichi; Ishii, Takaaki
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002000259	A1	20020103	WO 2001-JP5524	20010627
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001066342	A5	20020108	AU 2001-66342	20010627
	CA 2413506	A1	20021220	CA 2001-2413506	20010627
	EP 1295608	A1	20030326	EP 2001-943844	20010627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	HU 200301719	A2	20030929	HU 2003-1719	20010627
	BR 2001011976	A	20031209	BR 2001-11976	20010627
	EE 200200717	A	20040816	EE 2002-717	20010627
	NZ 523800	A	20050225	NZ 2001-523800	20010627
	BG 107371	A	20030829	BG 2002-107371	20021211
	US 2003186992	A1	20031002	US 2002-311429	20021218
	US 6949552	B2	20050927		
	NO 2002006122	A	20030225	NO 2002-6122	20021219
	ZA 2002010386	A	20040210	ZA 2002-10386	20021220

PRAI JP 2000-192856 A 20000627
WO 2001-JP5524 W 20010627
OS MARPAT 136:79788
GI



I

AB A remedy for anxiety neurosis or depression which contains an **melanocortin** MC4 receptor antagonist as the active ingredient; and a piperazine derivative represented by the formula [I] or a pharmaceutically acceptable salt thereof, wherein Ar1 represents (un)substituted Ph, etc.; Ar2 represents (un)substituted naphthyl, quinolyl, a group represented by the formula [a] (wherein R4 is hydrogen or halogeno; and X-Y is CH-NH, CH-O, CH-S, or N-O), or a group represented by the formula [b] (wherein R5 is hydrogen, hydroxy, or C1-10 alkoxy); R1 represents hydrogen, C1-10 alkyl, etc.; R2 and R3 are the same or different and each is hydrogen or C1-10 alkyl; A-B represents N-CH2, CH-CH2, C(OH)-CH2, or C=CH; T1 represents a single bond, -O-, etc.; and n is an integer of 1 to 10.

IC ICM A61K045-00
ICS A61K031-496; A61K031-495; A61P025-24; A61P025-22; C07D295-12; C07D239-42; C07D215-12; C07D307-81; C07D209-14; C07D333-20; C07D311-80; C07D261-20; C07D211-44; C07D211-70; C07D295-06; C07D295-02; C07D295-08; C07D295-14; C07D211-20

CC 1-11 (Pharmacology)
Section cross-reference(s): 28

ST anxiolytic antidepressant piperazine deriv **melanocortin** receptor

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin** receptor, MC4; remedial agent for anxiety neurosis or depression and piperazine derivative)

IT Mental and behavioral disorders
(neurosis; remedial agent for anxiety neurosis or depression and piperazine derivative)

IT Antidepressants
Anxiolytics
(remedial agent for anxiety neurosis or depression and piperazine derivative)

IT **385843-90-3P 385843-94-7P 385843-97-0P**
385844-01-9P 385844-03-1P 385844-05-3P
385844-07-5P 385844-09-7P 385844-10-0P
385844-11-1P 385844-13-3P 385844-20-2P
385844-23-5P 385844-26-8P 385844-29-1P
385844-30-4P 385844-31-5P 385844-32-6P
385844-36-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(remedial agent for anxiety neurosis or depression and piperazine derivative)

IT 108-18-9, Diisopropylamine 120-43-4, 1-Ethoxycarbonylpiperazine 121-44-8, Triethylamine, reactions 456-04-2, 2-Chloro-4'-

fluoroacetophenone 781-74-8, 1-Naphthalenebutanoic acid 7087-68-5, N-Ethyldiisopropylamine 14425-64-0, 4-Methoxyphenethylbromide 89011-82-5 385843-91-4 **385843-98-1 385843-99-2** 385844-16-6 385844-33-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(remedial agent for anxiety neurosis or depression and piperazine derivative)

IT 18511-62-1P, 2-(4-Fluorophenyl)oxirane 40336-01-4P 89011-47-2P 89011-51-8P 344579-12-0P **385843-92-5P 385843-93-6P 385843-95-8P 385843-96-9P** 385844-04-2P **385844-12-2P** 385844-14-4P 385844-15-5P **385844-17-7P 385844-18-8P 385844-19-9P 385844-21-3P 385844-22-4P 385844-24-6P 385844-25-7P 385844-27-9P 385844-28-0P 385844-34-8P 385844-35-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(remedial agent for anxiety neurosis or depression and piperazine derivative)

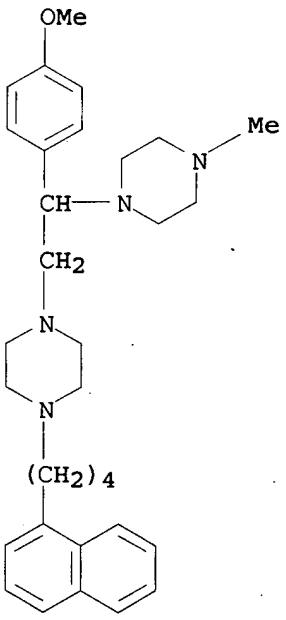
IT **385843-90-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(remedial agent for anxiety neurosis or depression and piperazine derivative)

RN 385843-90-3 HCAPLUS

CN Piperazine, 1-[2-(4-methoxyphenyl)-2-(4-methyl-1-piperazinyl)ethyl]-4-[4-(1-naphthalenyl)butyl]-, (2Z)-2-butenedioate (1:3) (9CI) (CA INDEX NAME)

CM 1

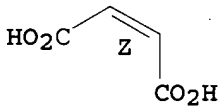
CRN 385843-89-0
CMF C32 H44 N4 O



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:713326 HCAPLUS
DN 135:272990
TI Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists
IN Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin; Lai, Yingjie; Nargund, Ravi P.; Park, Min K.; Pollard, Patrick G.; Sebhat, Iyassu K.; Ye, Zhixiong
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001070708	A1	20010927	WO 2001-US8935	20010320
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2403686	A1	20010927	CA 2001-2403686	20010320
	US 2002019523	A1	20020214	US 2001-812965	20010320
	US 6458790	B2	20021001		
	EP 1268449	A1	20030102	EP 2001-922501	20010320
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003528088	T	20030924	JP 2001-568918	20010320
PRAI	US 2000-191442P	P	20000323		
	US 2000-242265P	P	20001020		
	WO 2001-US8935	W	20010320		

OS MARPAT 135:272990
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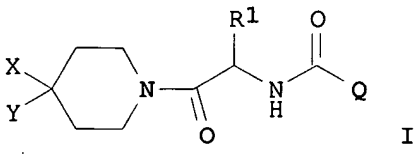

I

AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepared as **melanocortin**-4 receptor (MC-4R) agonists. Thus, capsule formulations containing title compound (II) were prepared
Representative
I activated MC-4R with IC50<1 μM. I are claimed for the treatment of obesity, diabetes, and sexual dysfunction including erectile dysfunction and female sexual dysfunction.

IC ICM C07D241-02
ICS C07D241-36; C07D401-00; C07D413-00; C07D487-00; A61K031-535; A61K031-495; A61K031-50; A61P015-10

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

ST piperazinylcarbonylaminomethylcarbonylpiperidine prepn **melanocortin** receptor agonist; sexual dysfunction treatment piperazinylcarbonylaminomethylcarbonylpiperidine; obesity treatment piperazinylcarbonylaminomethylcarbonylpiperidine; diabetes treatment piperazinylcarbonylaminomethylcarbonylpiperidine; piperidine piperazinylcarbonylaminomethylcarbonyl prepn **melanocortin** receptor agonist

IT Dopamine agonists
(combination therapy; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sexual behavior
(disorder, treatment; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Sexual behavior
(impotence, treatment; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(**melanocortin** 4, agonists; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Antidiabetic agents
Antiobesity agents
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Adrenoceptor antagonists
(α2-, combination therapy; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT Adrenoceptor agonists
(β3-, combination therapy; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 171596-29-5, IC-351 171599-83-0, Sildenafil citrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 363187-87-5P 363189-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT

363187-28-4P	363187-29-5P	363187-30-8P	363187-31-9P	363187-32-0P
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363189-53-1P	363189-54-2P	363189-55-3P	363189-56-4P	363189-57-5P
363189-58-6P	363189-59-7P	363189-60-0P	363189-61-1P	363189-62-2P
363189-63-3P	363189-89-3P	363189-90-6P	363189-91-7P	363189-92-8P
363189-93-9P	363189-94-0P	363189-95-1P	363189-96-2P	363189-97-3P
363189-98-4P	363189-99-5P	363190-00-5P	363190-01-6P	363190-02-7P
363190-03-8P	363190-04-9P	363190-05-0P	363190-06-1P	363190-07-2P
363190-08-3P	363190-09-4P	363190-10-7P	363190-11-8P	363190-12-9P

363190-13-0P 363190-14-1P 363190-15-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 363190-16-3P 363190-17-4P 363190-19-6P 363190-59-4P 363190-60-7P
363190-61-8P 363190-62-9P 363190-63-0P 363190-64-1P 363190-65-2P
363190-66-3P 363190-67-4P 363190-68-5P 363190-69-6P 363190-70-9P
363190-71-0P 363190-72-1P 363190-73-2P 363190-74-3P 363190-75-4P
363190-76-5P 363190-77-6P 363190-78-7P 363190-79-8P 363190-80-1P
363190-81-2P 363190-82-3P 363190-83-4P 363190-84-5P 363190-85-6P
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363190-96-9P 363190-97-0P 363190-98-1P 363190-99-2P 363191-07-5P
363191-08-6P 363191-09-7P 363191-13-3P 363191-15-5P 363191-16-6P
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363191-42-8P 363191-43-9P 363191-44-0P 363191-45-1P 363191-46-2P
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363191-90-6P 363191-92-8P 363192-00-1P 363192-01-2P 363192-06-7P
363192-15-8P 363192-17-0P 363192-82-9P 363620-30-8P 363620-31-9P
363620-34-2P 363620-36-4P 363620-38-6P 363620-40-0P 363620-41-1P
363620-43-3P 363620-45-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

IT 75-44-5, Phosgene 75-64-9, tert-Butylamine, reactions 95-89-6, 3-Chloro-2,5-dimethylpyrazine 110-85-0, Piperazine, reactions 124-68-5 535-11-5, Ethyl 2-bromopropionate 556-82-1, 3-Methyl-2-buten-1-ol 565-69-5, Ethyl isopropyl ketone 598-21-0 811-93-8, 1,2-Diamino-2-methylpropane 1067-74-9, Methyl diethylphosphonoacetate 1193-18-6 1436-59-5, cis-1,2-Diaminocyclohexane 2749-11-3, (S)-2-Amino-1-propanol 3674-13-3, Ethyl 2,3-dibromopropionate 5521-55-1, 5-Methyl-2-pyrazinecarboxylic acid 5521-61-9, 6-Methyl-2-pyrazinecarboxylic acid 6294-40-2 7051-34-5, Cyclopropylmethyl bromide 7764-95-6 10316-79-7 20607-43-6, Sodium isopropylsulfide 22059-21-8, 1-Aminocyclopropane-1-carboxylic acid 29460-90-0, 2-Isopropylpyrazine 35761-26-3 45767-66-6, 2-Chloro-4-fluorobenzyl bromide 57292-44-1 57292-45-2 62234-36-0 69555-14-2 83949-32-0 84358-13-4 92329-61-8 129799-15-1 138775-02-7 138775-03-8 139631-62-2, Cyclopropylsulfonyl chloride 142851-03-4 312638-87-2 363192-22-7 363192-64-7 363192-65-8 363192-66-9 363192-73-8 363192-76-1 363192-79-4 363192-81-8 363192-86-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

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363192-38-5P 363192-39-6P 363192-40-9P 363192-41-0P 363192-42-1P
363192-43-2P 363192-44-3P 363192-45-4P 363192-46-5P 363192-47-6P
363192-48-7P 363192-49-8P 363192-50-1P 363192-51-2P 363192-52-3P
363192-53-4P 363192-54-5P 363192-55-6P 363192-56-7P 363192-57-8P
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363192-63-6P 363192-67-0P 363192-68-1P 363620-42-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

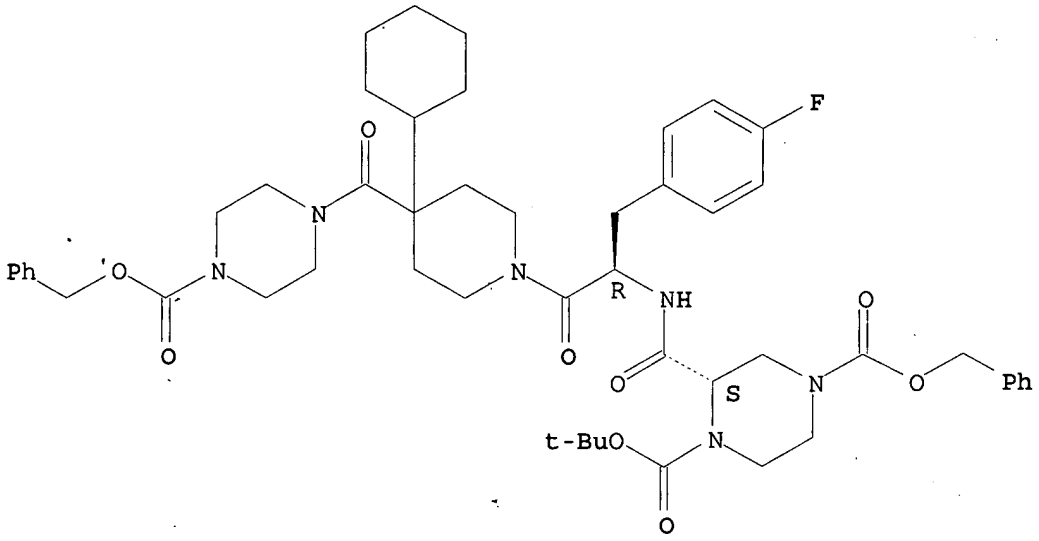
IT **363189-30-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as **melanocortin**-4 receptor agonists)

RN 363189-30-4 HCAPLUS

CN 1,4-Piperazinedicarboxylic acid, 2-[[[(1R)-2-[4-cyclohexyl-4-[[4-[(phenylmethoxy)carbonyl]-1-piperazinyl]carbonyl]-1-piperidinyl]-1-[(4-fluorophenyl)methyl]-2-oxoethyl]amino]carbonyl]-, 1-(1,1-dimethylethyl) 4-(phenylmethyl) ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:713201 HCAPLUS
DN 135:267270
TI Spiropiperidine derivatives as **melanocortin** receptor agonists
IN Palucki, Brenda L.; Nargund, Ravi P.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001070337	A1	20010927	WO 2001-US8833	20010320
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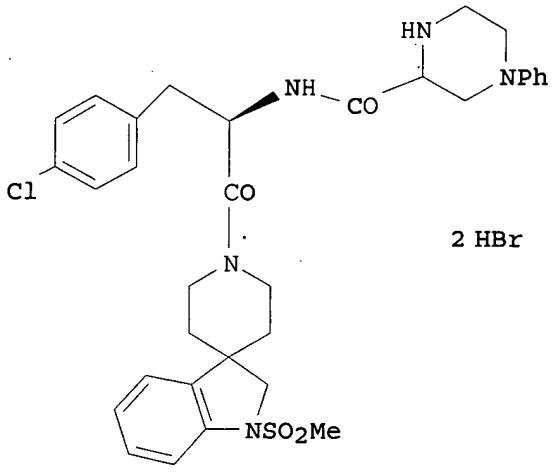
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2403631	A1	20010927	CA 2001-2403631	20010320
	US 6472398	B1	20021029	US 2001-812339	20010320
	EP 1268000	A1	20030102	EP 2001-922484	20010320
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003527444	T	20030916	JP 2001-568527	20010320
PRAI	US 2000-191669P	P	20000323		
	WO 2001-US8833	W	20010320		

OS MARPAT 135:267270
GI



I

AB Certain novel spiropiperidine derivs. are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin**-4 receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. I was prepared and pharmacol. tests are described.

IC ICM A61P015-00
ICS A61P015-10; A61K031-535; A61K031-54; A61K031-495; A61K031-50; A61K031-55; C07D223-14; C07D401-00; C07D413-00; C07D417-00

CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 28, 63

ST spiropiperidine deriv prepn **melanocortin** receptor agonist

IT Sexual behavior
(disorder; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Sexual behavior
(impotence; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**melanocortin**; spiropiperidine derivs. as **melanocortin** receptor agonists)

IT Antidiabetic agents
Antiobesity agents
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 128908-32-7, **Melanocortin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT **126937-41-5** 138775-03-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT **126937-42-6P 126937-43-7P** 362513-36-8DP, acyl derivs.
362513-73-3P 362513-74-4P 362513-76-6P 362513-77-7P 362513-79-9P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 362513-35-7P 362513-36-8P 362513-37-9P 362513-38-0P 362513-39-1P
362513-40-4P 362513-41-5P 362513-42-6P 362513-43-7P 362513-44-8P
362513-45-9P 362513-46-0P 362513-47-1P 362513-48-2P 362513-49-3P

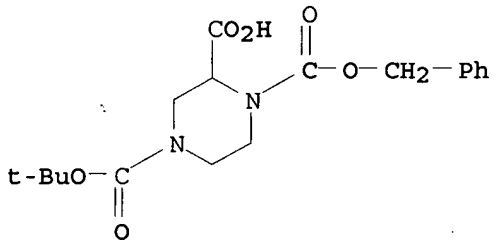
362513-50-6P 362513-51-7P 362513-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT 362513-53-9P 362513-54-0P 362513-55-1P 362513-56-2P 362513-57-3P
362513-58-4P 362513-59-5P 362513-60-8P 362513-61-9P 362513-62-0P
362513-63-1P 362513-64-2P 362513-65-3P 362513-66-4P 362513-67-5P
362513-68-6P 362513-69-7P 362513-70-0P 362513-71-1P 362513-72-2P
362513-78-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiropiperidine derivs. as **melanocortin** receptor agonists)

IT **126937-41-5**
RL: RCT (Reactant); RACT (Reactant or reagent); **PREP (Preparation)**
(spiropiperidine derivs. as **melanocortin** receptor agonists)

RN 126937-41-5 HCAPLUS

CN 1,2,4-Piperazinetricarboxylic acid, 4-(1,1-dimethylethyl) 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:565002 HCAPLUS
DN 135:152713
TI Aromatic amides as novel **melanocortin** receptor agonists and antagonists
IN Lundstedt, Torbjoern; Skottner, Anna; Seifert, Elisabeth; Starchenkov, Igor; Trapencieris, Peteris; Kauss, Valerjans; Kalvins, Ivars; Boman, Arne
PA Melacure Therapeutics AB, Swed.
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001055106	A2	20010802	WO 2001-GB346	20010129
	WO 2001055106	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2398728	A1	20010802	CA 2001-2398728	20010129
BR	2001007893	A	20021105	BR 2001-7893	20010129
EP	1254114	A2	20021106	EP 2001-946850	20010129
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JP	2003520850	T	20030708	JP 2001-555048	20010129
ZA	2002005886	A	20040621	ZA 2002-5886	20020723
US	2003195212	A1	20031016	US 2002-182192	20021120
PRAI	GB 2000-1948	A	20000128		
	GB 2000-2060	A	20000128		
	WO 2001-GB346	W	20010129		

OS MARPAT 135:152713

AB The present invention relates to novel aromatic amides (I; B-E-X-N(R8)-C(O)-Y-F-A and pharmacol. active salts thereof) and to the use of these amides for the treatment of obesity, anorexia, inflammation, mental disorders and other diseases associated with the **melanocortin** receptors or related systems, e.g. the melanocyte stimulating hormones. In I: E and F are independently a saturated or unsatd., acyclic hydrocarbon group having 1-5 C atoms. X and Y are independently methylene; one of X and Y are absent (i.e. a single bond); or X can be -CH(QR10)- and/or Y can be -CH(MR9)- (M and Q are independently a saturated or unsatd., straight or branched chain acyclic hydrocarbon group with 1-6 C atoms; or M and/or Q are absent (i.e. M and/or Q are single bonds)). R8, R9 and R10 are H, -PR4, -C(O)DR4 (P and D are independently a saturated or unsatd., straight or branched chain acyclic hydrocarbon group having 1-6 C atoms; or D is absent (i.e. D is a single bond)). R4 is hydroxy, Me, cyclohexyl, cyclopentyl, aminoguanidine, guanidine, carboxy, or (possibly substituted) amino, carbamoyl, alkoxy, alkoxycarbonyl, acyl, morpholinyl, pyrrolidinyl, piperidinyl, piperazinyl, Ph, isoindolyl, indenyl, pyridinyl, indolyl, pyrrolyl, cyclopentadienyl wherein R4 in R8, R9 and R10 may be the same or different. A and B are the same or different and are (possibly substituted) quinolinyl, isoquinolinyl, isoindolyl, naphthyl, pyridinyl, indolyl, pyrazinyl, cyclopentadienyl, pyrimidinyl, Ph, indenyl. Several claimed compds. (N-(3-aminopropyl)-3-(1H-indol-3-yl)-2-(2-naphthalen-1-ylacetylamino)propionamide hydrochloride (1:1.2), N-[1-[benzyl(4-guanidinobutyl)carbamoyl]-2-(1H-indol-3-yl)ethyl]-4-phenylbutyramide monohydrochloride, N-benzyl-N-(4-guanidinobutyl)-3-(1H-indol-3-yl)-2-(2-naphthalen-2-ylacetylamino)propionamide monohydrochloride, N-[1-(9-ethyl-9H-carbazol-3-ylcarbamoyl)-2-(1H-indol-3-yl)ethyl]-4-guanidinobutyramide monohydrochloride, 4-amino-N-[1-(9-ethyl-9H-carbazol-3-ylcarbamoyl)-2-(1H-indol-3-yl)ethyl]butyramide monohydrochloride, 2-(3-aminopropionylamino)-N-(9-ethyl-9H-carbazol-3-yl)-3-(1H-indol-3-yl)propionamide monohydrochloride) were tested (results given) for affinity for **melanocortin** receptors (MC1, MC3, MC4, MC5) and/or influence on cAMP. In vivo effects on food intake and anti-inflammatory effects were also determined on selected compds. Two example prepns. are given.

IC ICM C07D209-00

CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 34, 63

ST arom amide **melanocortin** receptor agonist antagonist prepn; antiobesity agent arom amide; antiinflammatory agent arom amide; mental disorder drug arom amide; anorexia drug arom amide; indolyl carboxamide **melanocortin** receptor agonist antagonist prepn

IT Allergy inhibitors
Analgesics
Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents

Cardiovascular agents
(aromatic amides as)
IT Skin
(aromatic amides useful for inducing tanning and lightening of)
IT Anorexia
Ischemia
Mental disorder
Reperfusion
(aromatic amides useful for treating)
IT Endocrine system
(aromatic amides useful for treating dysfunctions of)
IT Amides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aryl; preparation and use as novel **melanocortin** receptor agonists and antagonists)
IT Sexual behavior
(disorder; aromatic amides useful for treating)
IT Disease, animal
(drug-induced; aromatic amides useful for treating)
IT Drug delivery systems
(for aromatic amides useful as **melanocortin** receptor agonists and antagonists)
IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin**; aromatic amides as novel **melanocortin** receptor agonists and antagonists)
IT Antitumor agents
(melanoma; aromatic amides as)
IT Antitumor agents
(metastasis; aromatic amides as)
IT Amides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolyl- and other functional group-containing amides and use as
novel **melanocortin** receptor agonists and antagonists)
IT Nerve
(regeneration; aromatic amides useful for inducing)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tryptophan-containing; aromatic amides as novel **melanocortin** receptor agonists and antagonists and their preparation)
IT 128908-32-7, **Melanocortin**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(aromatic amides as novel **melanocortin** receptor agonists and antagonists)
IT 553-06-0P, N-(1,2-Diphenylethyl)nicotinamide 10254-15-6P 352276-87-0P
352276-88-1P 352276-89-2P 352276-90-5P 352276-91-6P 352276-94-9P
352276-96-1P 352276-98-3P 352277-00-0P 352277-02-2P 352277-04-4P
352277-06-6P 352277-08-8P 352277-10-2P 352277-12-4P 352277-14-6P
352277-16-8P 352277-18-0P 352277-20-4P 352277-22-6P 352277-24-8P
352277-26-0P 352277-28-2P 352277-30-6P 352277-32-8P 352277-34-0P
352277-36-2P 352277-38-4P 352277-40-8P 352277-42-0P 352277-44-2P

352277-46-4P 352277-49-7P 352277-51-1P 352277-54-4P 352277-56-6P
352277-58-8P 352277-60-2P 352277-62-4P 352277-63-5P 352277-64-6P
352277-65-7P 352277-66-8P 352277-68-0P 352277-70-4P 352277-72-6P
352277-73-7P 352277-74-8P 352277-75-9P 352277-76-0P 352277-77-1P
352277-78-2P 352277-79-3P 352277-81-7P 352277-83-9P 352277-85-1P
352277-87-3P 352277-88-4P 352277-90-8P 352277-92-0P 352277-94-2P
352277-96-4P 352277-97-5P 352277-99-7P 352278-01-4P 352278-03-6P
352278-04-7P 352278-05-8P 352278-06-9P 352278-07-0P 352278-09-2P
352278-11-6P 352278-19-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(aromatic amides as novel **melanocortin** receptor agonists and antagonists and their preparation)

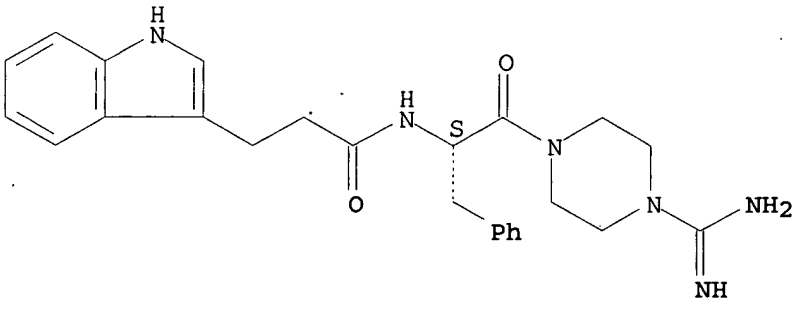
IT 60722-88-5P 352278-13-8P **352278-16-1P** 352278-22-9P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; aromatic amides as novel **melanocortin** receptor agonists and antagonists and their preparation)

IT 73-22-3, L-Tryptophan, reactions 110-85-0, Piperazine, reactions 830-96-6D, 3-(1H-Indol-3-yl)propionic acid, activated ester 2038-57-5, (3-Phenylpropyl)amine 5105-78-2, 4-Benzyloxycarbonylaminobutyric acid 6066-82-6, N-Hydroxysuccinimide 25508-20-7 75048-11-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; aromatic amides as novel **melanocortin** receptor agonists and antagonists and their preparation)

IT **352278-11-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **PREP (Preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(aromatic amides as novel **melanocortin** receptor agonists and antagonists and their preparation)

RN 352278-11-6 HCAPLUS
CN 1H-Indole-3-propanamide, N-[(1S)-2-[4-(aminoiminomethyl)-1-piperazinyl]-2-oxo-1-(phenylmethyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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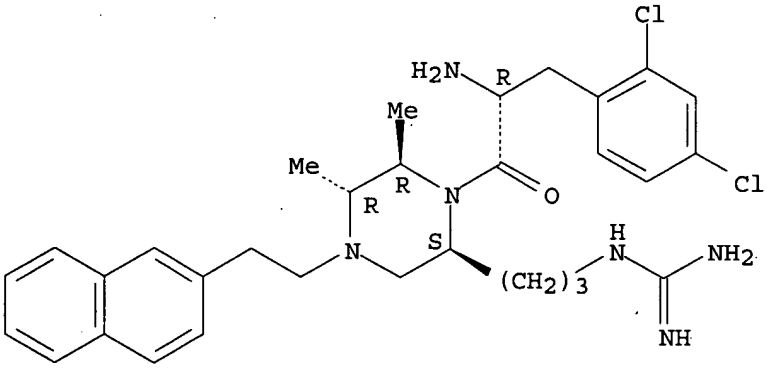
L3 ANSWER 1 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791625-47-3 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5,6-dimethyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R,6R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H40 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

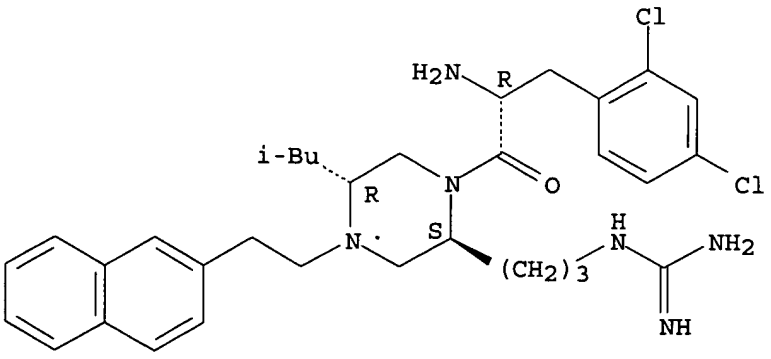


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-99-2 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-(2-methylpropyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H44 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

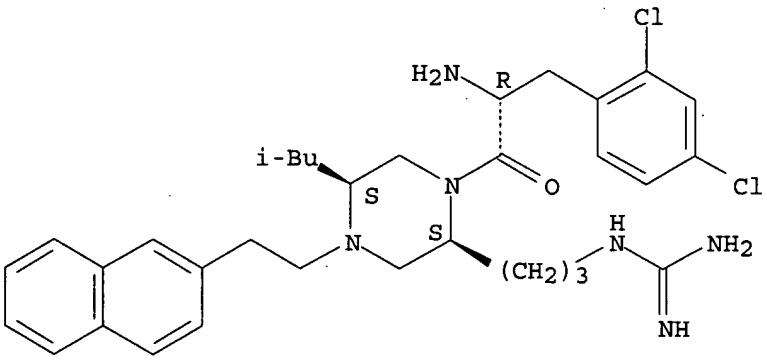


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-98-1 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-(2-methylpropyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S,5S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H44 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

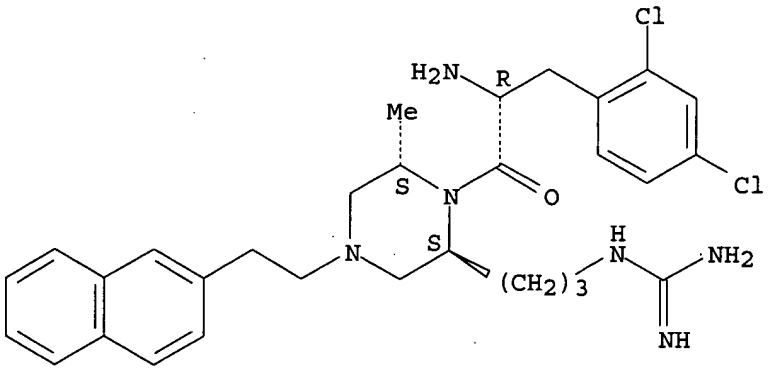


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-95-8 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H38 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

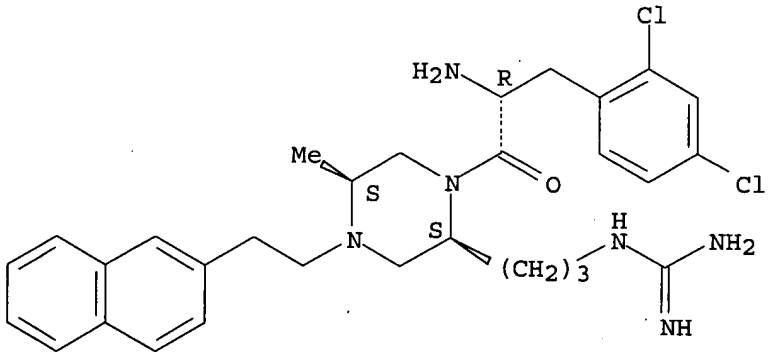


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-93-6 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H38 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



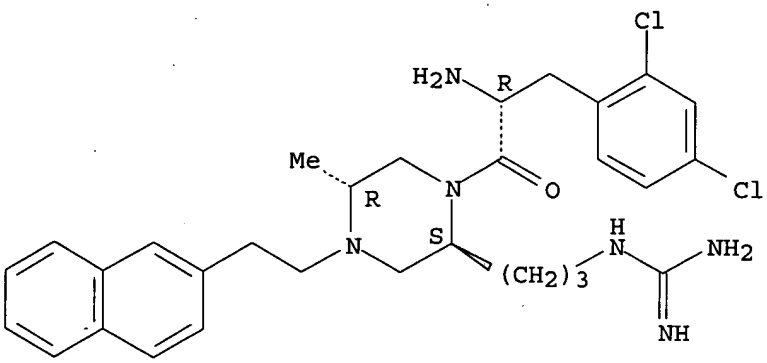
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 6 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-91-4 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H38 Cl2 N6 O
SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

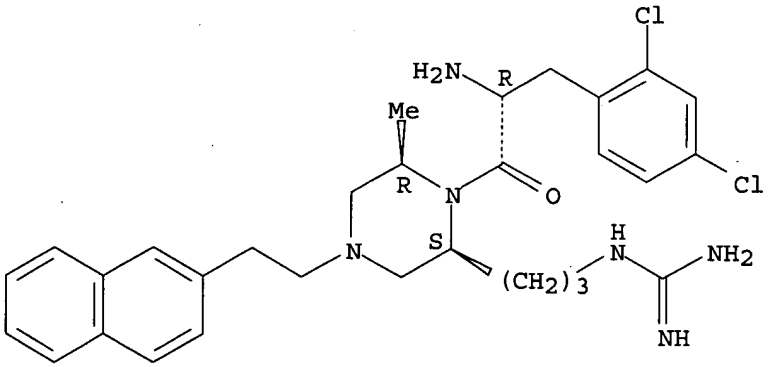


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 791624-89-0 REGISTRY
ED Entered STN: 02 Dec 2004
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H38 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



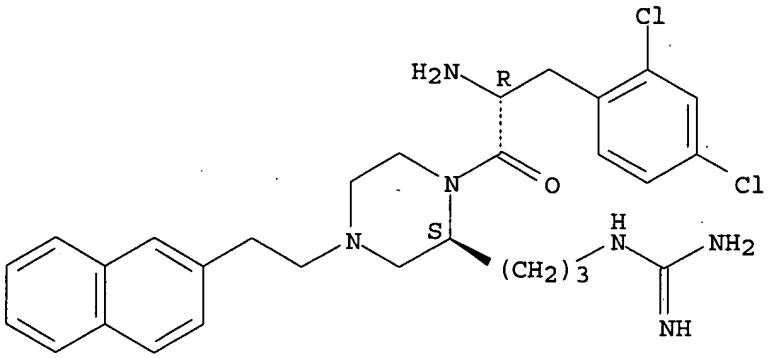
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 8 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 497935-98-5 REGISTRY
ED Entered STN: 12 Mar 2003
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S)- (9CI)

(CA INDEX NAME)
FS STEREOSEARCH
MF C29 H36 Cl2 N6 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

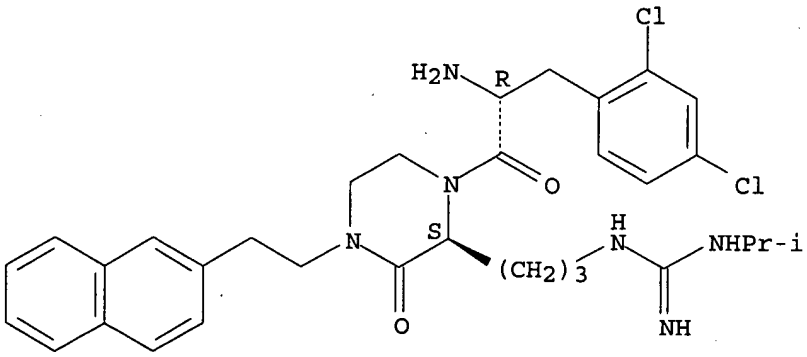


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 9 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 497935-44-1 REGISTRY
ED Entered STN: 12 Mar 2003
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino[(1-methylethyl)amino]methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H40 Cl2 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



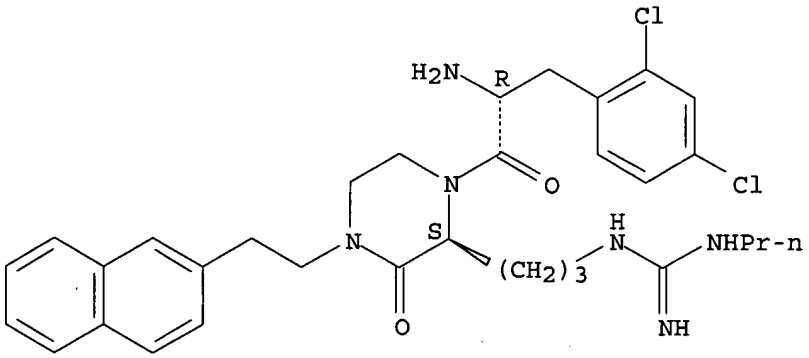
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN

RN 497935-43-0 REGISTRY
ED Entered STN: 12 Mar 2003
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(propylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H40 Cl2 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

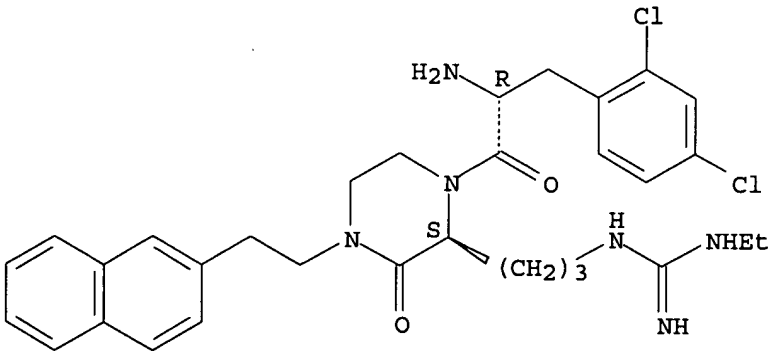


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 497935-42-9 REGISTRY
ED Entered STN: 12 Mar 2003
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[(ethylamino)iminomethyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H38 Cl2 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

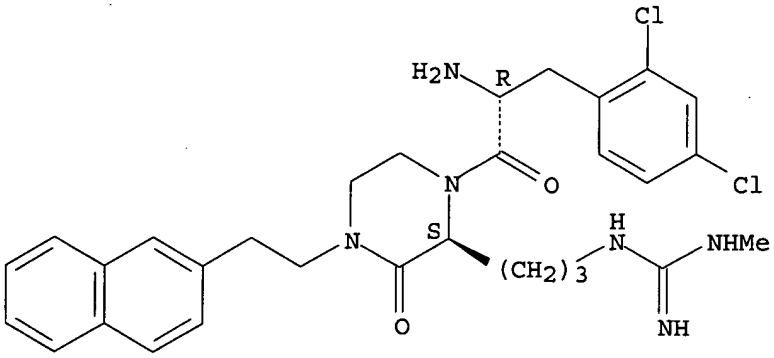


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 497935-41-8 REGISTRY
ED Entered STN: 12 Mar 2003
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(methylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H36 Cl2 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

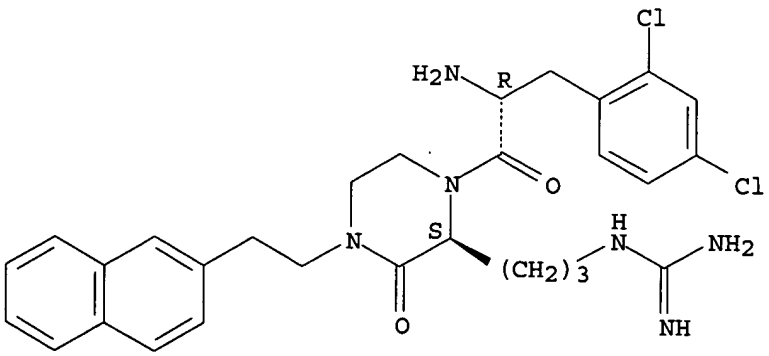


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2007 ACS on STN
RN 497935-20-3 REGISTRY
ED Entered STN: 12 Mar 2003
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[(aminoiminomethyl)amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H34 Cl2 N6 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	198.35	198.56

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FILE COVERS 1907 - 26 Jan 2007 VOL 146 ISS 6
FILE LAST UPDATED: 25 Jan 2007 (20070125/ED)

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FILE 'REGISTRY' ENTERED AT 13:59:20 ON 26 JAN 2007
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 13 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:01:10 ON 26 JAN 2007

=> s l3
L4 4 L3

=> d ibib abs hitstr 1-4

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:527392 CAPLUS
DOCUMENT NUMBER: 143:20084
TITLE: Naphthalene-containing melanocortin receptor-specific small molecule
INVENTOR(S): Sharma, Shubh D.; Shadiack, Annette M.; Shi, Yi-Qun; Wu, Zhijun; Rajpurohit, Ramesh; Burris, Kevin; Purma, Papireddy
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 837,519.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005130988	A1	20050616	US 2005-36282	20050114
WO 2003013571	A1	20030220	WO 2002-US25574	20020812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152134	A1	20040805	US 2004-761889	20040121
US 2004157264	A1	20040812	US 2004-762079	20040121
WO 2005102340	A1	20051103	WO 2004-US1462	20040121
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004224957	A1	20041111	US 2004-837519	20040430

PRIORITY APPLN. INFO.:		
US 2001-311404P	P	20010810
WO 2002-US25574	A2	20020812
US 2003-467442P	P	20030501
US 2003-474497P	P	20030530
US 2004-536606P	P	20040114
US 2004-761889	A2	20040121
US 2004-762079	A2	20040121
US 2004-546393P	P	20040219
US 2004-559741P	P	20040405
US 2004-563739P	P	20040419
US 2004-837519	A2	20040430

OTHER SOURCE(S): MARPAT 143:20084

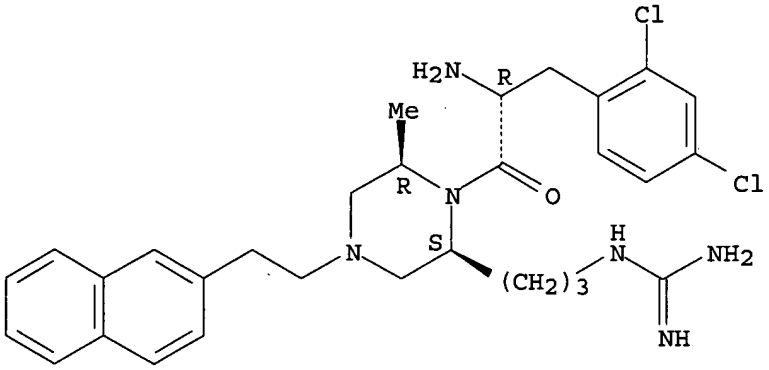
AB A method of modulating energy homeostasis in a mammal without eliciting a sexual response by administration of a therapeutically effective amount of a pharmaceutical composition including a melanocortin receptor compound of the formula I (where R1 = a bond or a linker unit including from one to six backbone atoms and an unsubstituted naphthalene group, L = a conformationally restricted ring system consisting of a single ring or bicyclic nonarom. carbocyclic ring system, etc., R2= -(CH2)4NH2,-(CH2)3NHC(NH2)=NH, etc., R3 = L-or D-isomer of Phe, Phe(4-F), Phe(4-Br), etc., and Rx = H, C-C6 aliphatic linear chain, etc.).

IT 791624-89-0P 791624-91-4P 791624-95-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(naphthalene-containing melanocortin receptor-specific small mol.)

RN 791624-89-0 CAPLUS

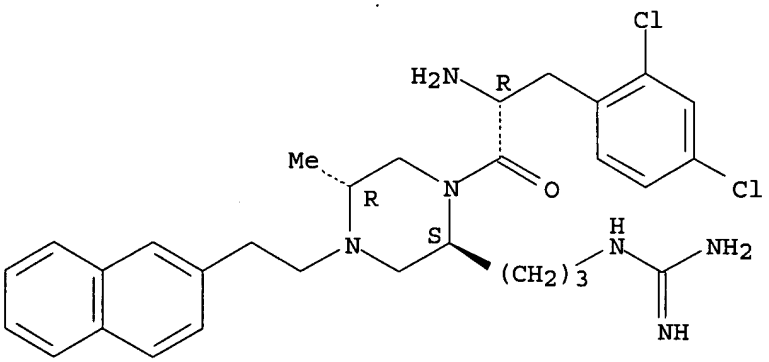
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



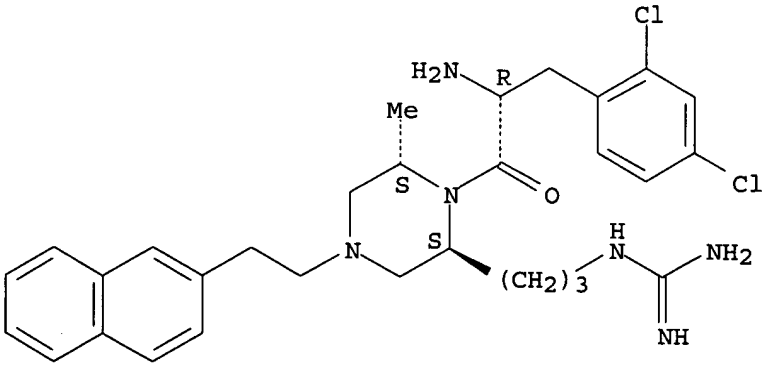
RN 791624-91-4 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 791624-95-8 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:965987 CAPLUS

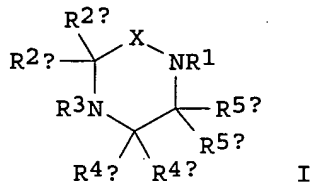
DOCUMENT NUMBER: 141:411221
TITLE: Preparation of piperazine melanocortin receptor-specific compounds
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-qun; Rajpurohit, Ramesh; Wu, Zhijun; Purma, Papireddy; Shadiack, Annette M.; Burris, Kevin D.
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 69 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004224957	A1	20041111	US 2004-837519	20040430
AU 2004235792	A1	20041118	AU 2004-235792	20040503
WO 2004098602	A1	20041118	WO 2004-US13803	20040503
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1622618	A1	20060208	EP 2004-751262	20040503
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004010694	A	20060620	BR 2004-10694	20040503
CN 1816337	A	20060809	CN 2004-80018907	20040503
JP 2006525369	T	20061109	JP 2006-514263	20040503
US 2005130988	A1	20050616	US 2005-36282	20050114
US 2005124636	A1	20050609	US 2005-40838	20050121
US 2005176728	A1	20050811	US 2005-99814	20050405
US 2006287330	A1	20061221	US 2006-464051	20060811
US 2006287331	A1	20061221	US 2006-464053	20060811
US 2006287332	A1	20061221	US 2006-464069	20060811

PRIORITY APPLN. INFO.:

US 2003-467442P	P	20030501
US 2004-546393P	P	20040219
US 2001-311404P	P	20010810
WO 2002-US25574	A2	20020812
US 2003-474497P	P	20030530
US 2004-536606P	P	20040114
US 2004-538100P	P	20040121
US 2004-761889	A2	20040121
US 2004-762079	A2	20040121
US 2004-559741P	P	20040405
US 2004-563739P	P	20040419
US 2004-837519	A	20040430
WO 2004-US13803	W	20040503
US 2005-707488P	P	20050811

OTHER SOURCE(S): MARPAT 141:411221
GI



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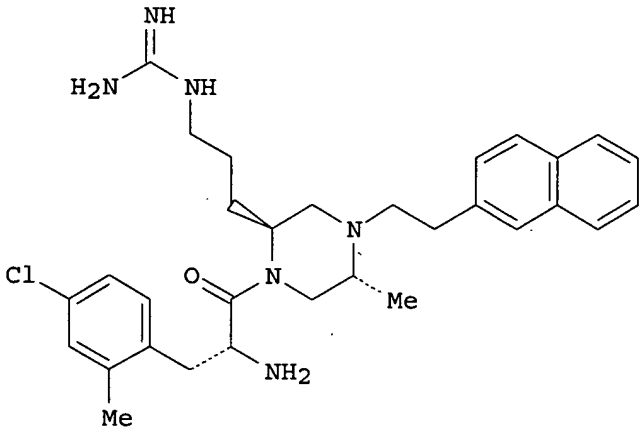


II

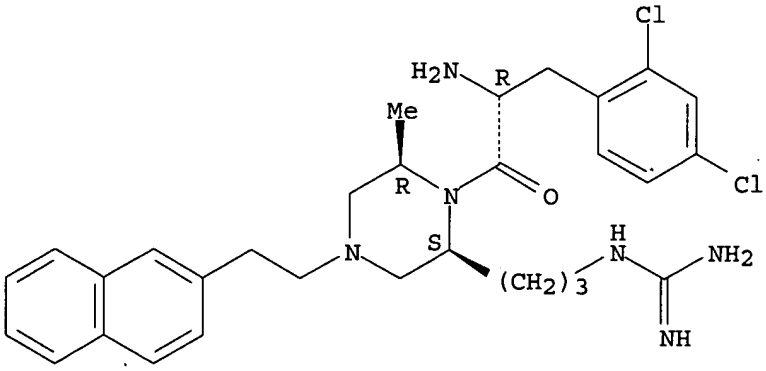
AB The invention relates to amino acid-derived piperazine compds. I [X is CH2, CO or CS; R1 is -L1-J; one of R2a and R2b is -L2-W and the other is H; R3 is -L3-Q; L1 is a bond or a linker unit comprising from one to eight backbone atoms selected from carbon, sulfur, oxygen or nitrogen; J is a ring structure, e.g., an (un)substituted aromatic or non-aromatic carbocyclic ring; L2 is a bond or (CH2)1-6; W is a heteroatom unit with at least one cationic center, hydrogen bond donor or acceptor (at least one heteroatom is nitrogen or oxygen); L3 is a bond or a linker unit comprising from one to nine backbone atoms selected from carbon, sulfur, oxygen or nitrogen; Q is (un)substituted Ph or naphthyl; one or two of R4a, R4b, R5a and R5b are independently -L2-W or an aliphatic chain and the others are H, provided that at least one of R4a and R4b and at least one of R5a and R5b is H], including enantiomers, stereoisomers, diastereoisomers or pharmaceutically-acceptable salts, which bind with high affinity to one or more melanocortin receptors (MCR) and may be employed for treatment of melanocortin receptor-associated conditions or disorders. Thus, piperazine derivative II was prepared via reactions of 2-naphthylacetic acid, (R)-(-)-2-amino-1-propanol, Fmoc-L-Arg(Boc)2-OH (Fmoc = fluorenylmethoxycarbonyl, Boc = tert-butoxycarbonyl), and Boc-D-4-chloro-2-methyl-L-phenylalanine. Compound II was shown to be a partial agonist as to MC4-R and in rats caused a decrease in food intake (administration 2 h prior to food presentation) and induced penile erection at 0.3-30 μg/Kg.

IT 791624-89-0P 791624-91-4P 791624-93-6P
791624-95-8P 791624-98-1P 791624-99-2P
791625-47-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine melanocortin receptor-specific compds.)

RN 791624-89-0 CAPLUS

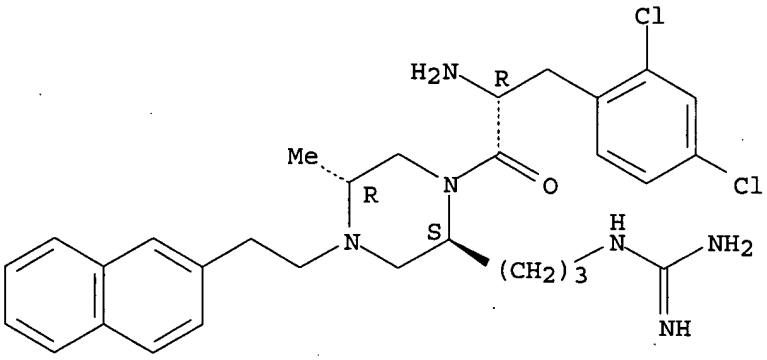
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



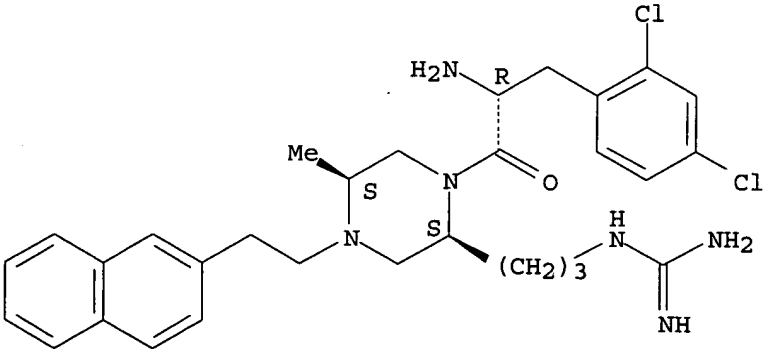
RN 791624-91-4 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



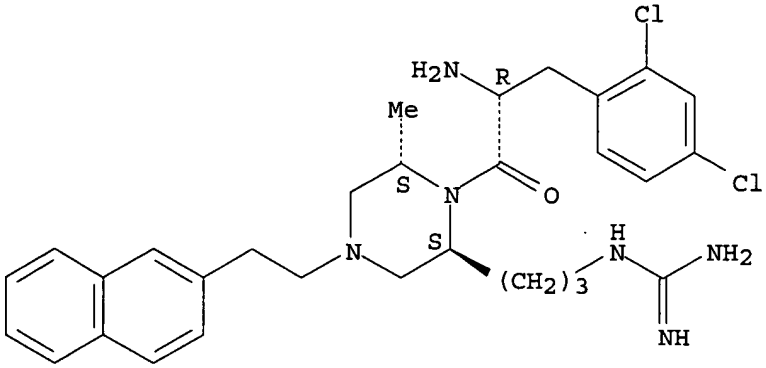
RN 791624-93-6 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



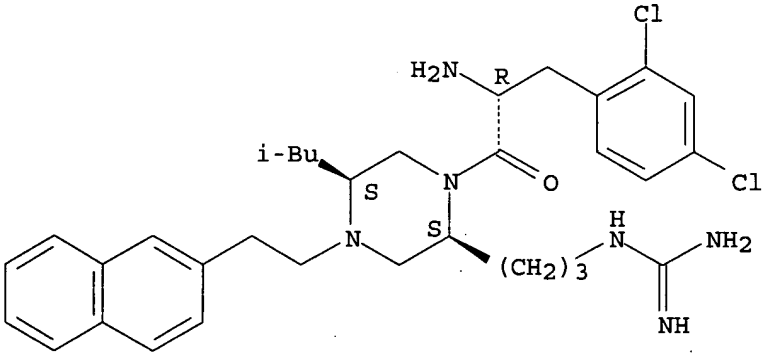
RN 791624-95-8 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-6-methyl-4-[2-(2-naphthalenyl)ethyl]-, (2S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



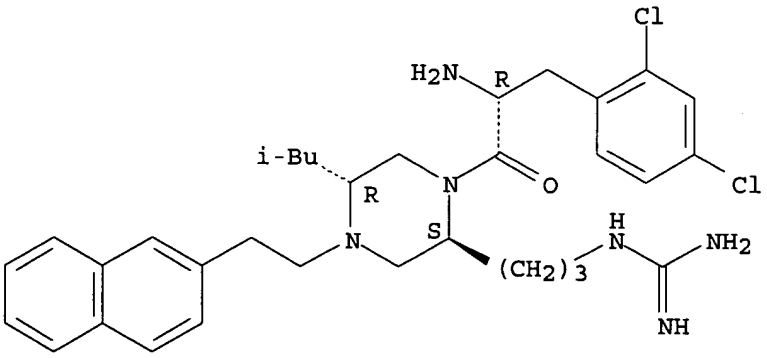
RN 791624-98-1 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-(2-methylpropyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 791624-99-2 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5-(2-methylpropyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S,5R)- (9CI) (CA INDEX NAME)

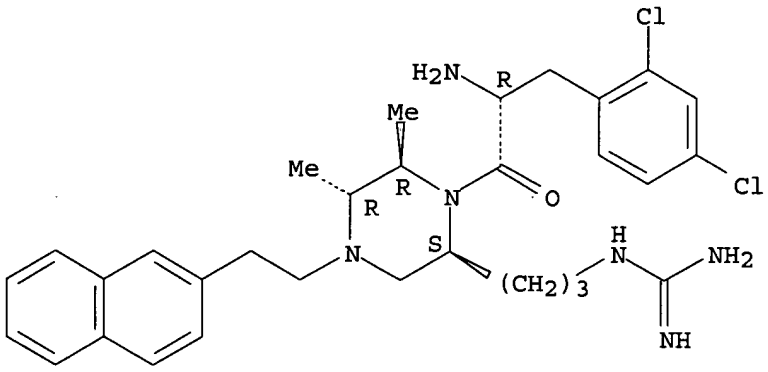
Absolute stereochemistry.



RN 791625-47-3 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-5,6-dimethyl-4-[2-(2-naphthalenyl)ethyl]-,

(2S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:652533 CAPLUS
DOCUMENT NUMBER: 141:191073
TITLE: Preparation of piperazines as melanocortin-specific agonists, antagonists, or mixed agonists and antagonists.
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-qun; Wu, Zhijun; Rajpurohit, Ramesh
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 70 pp., Cont.-in-part of Appl. No. PCT/US02/25574.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004157264	A1	20040812	US 2004-762079	20040121
WO 2003013571	A1	20030220	WO 2002-US25574	20020812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2005102340	A1	20051103	WO 2004-US1462	20040121
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US 2005130988	A1	20050616	US 2005-36282	20050114
US 2005124636	A1	20050609	US 2005-40838	20050121

US 2005176728	A1	20050811	US 2005-99814	20050405
PRIORITY APPLN. INFO.:			US 2001-311404P	P 20010810
			WO 2002-US25574	A2 20020812
			US 2003-474497P	P 20030530
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			US 2004-536606P	P 20040114
			US 2004-538100P	P 20040121
			US 2004-761889	A2 20040121
			US 2004-762079	A2 20040121
			US 2004-546393P	P 20040219
			US 2004-559741P	P 20040405
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			US 2004-837519	A2 20040430

OTHER SOURCE(S): MARPAT 141:191073

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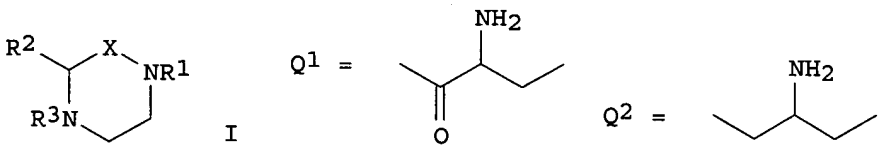
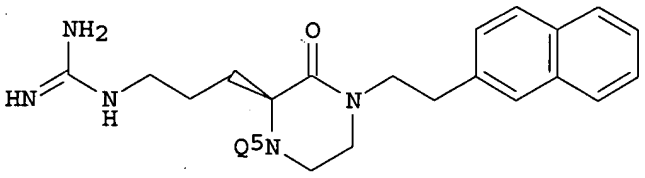




II

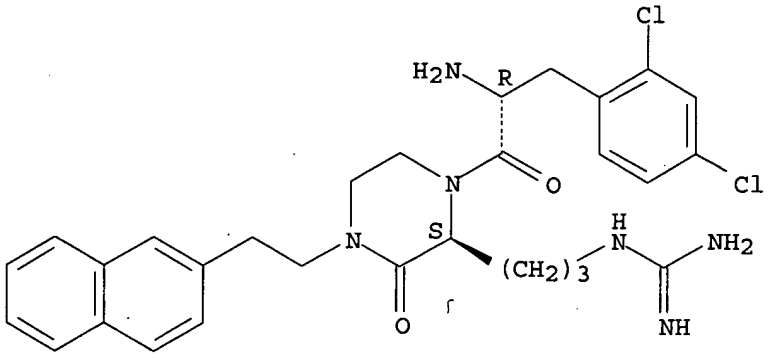
AB Title compds. [I; R1 = L1J, H; R2 = (CH2)yW, J, L1J; R3 = L2Q; L1 = (CH2)y, O(CH2)y, NH(CH2)y, CO(CH2)y, CO2(CH2)y, CH2CONH; J = (substituted) aryl, carbocyclyl, carbobicyclyl, heterobicyclyl; W = heteroatom unit with ≥1 cationic center, hydrogen bond donor, or hydrogen bond acceptor wherein ≥1 atom = N; L2 = Q1, Q2, Q3, Q4, etc.; Q = (substituted) Ph, naphthyl; R4 = H, R5, R5R6; R5 = amino acid residue, amine capping group; R6 = H, amine capping group; y = 1-6], were prepared Thus, title compound (II; Q5 = 2,4-dichloro-D-phenylalanyl) (general preparation given) at 1 μM gave 95% inhibition of melanocortin MC4-R.

IT 497935-20-3P 497935-41-8P 497935-42-9P
497935-43-0P 497935-44-1P 497935-98-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazines as melanocortin-specific agonists, antagonists, or mixed agonists and antagonists)

RN 497935-20-3 CAPLUS

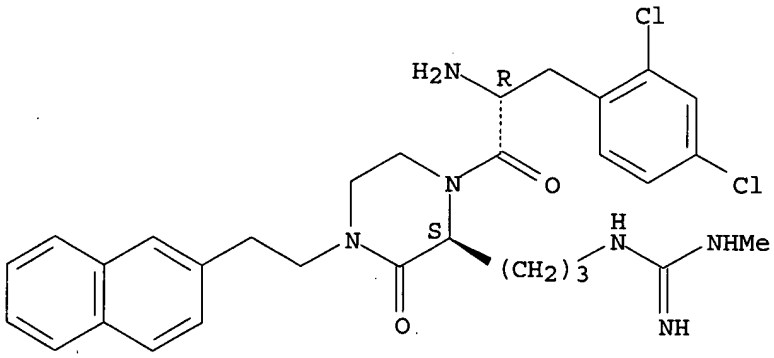
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[(aminoiminomethyl)amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



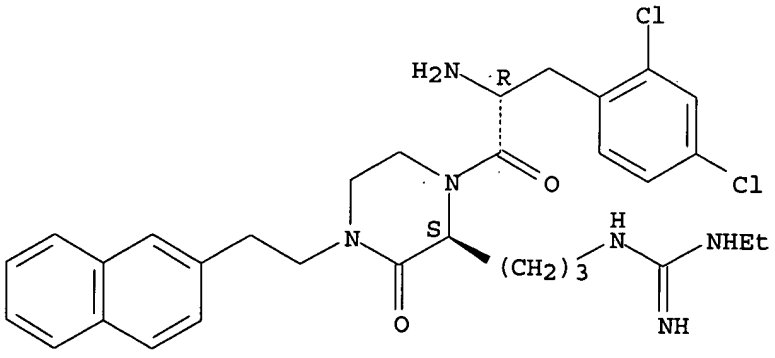
RN 497935-41-8 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(methylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 497935-42-9 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[(ethylamino)iminomethyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

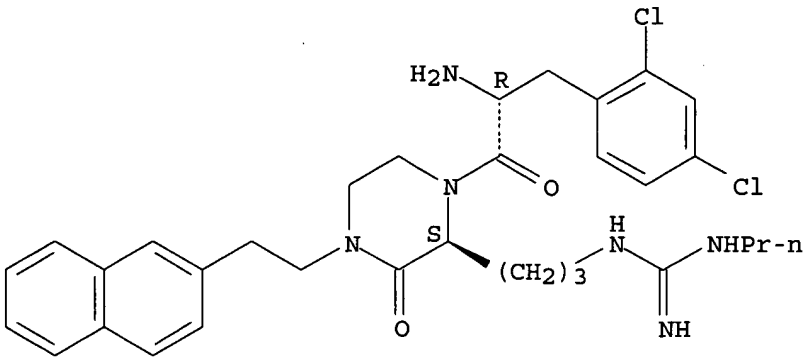
Absolute stereochemistry.



RN 497935-43-0 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(propylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-,

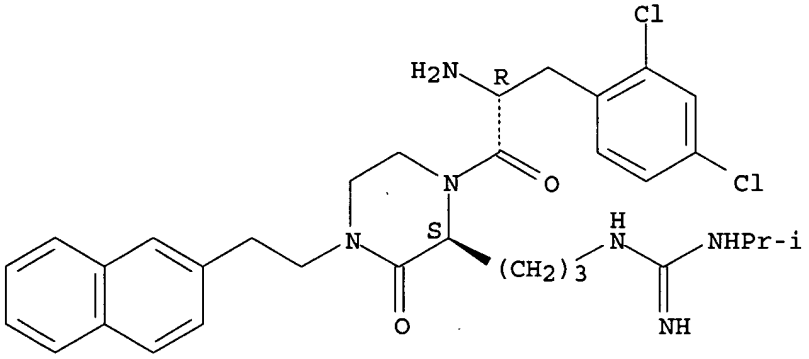
(3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



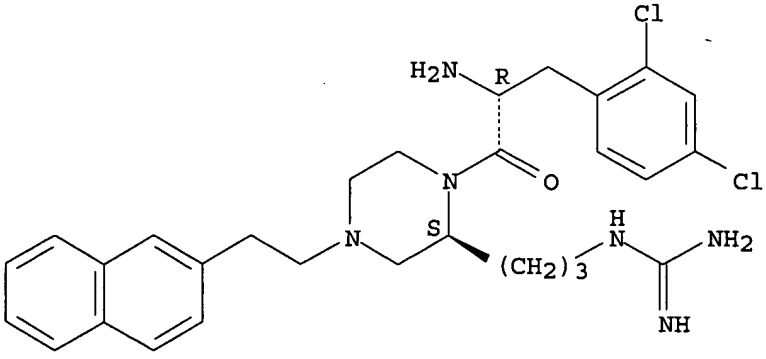
RN 497935-44-1 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino[(1-methylethyl)amino]methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 497935-98-5 CAPLUS
CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:133079 CAPLUS
DOCUMENT NUMBER: 138:188071
TITLE: Peptidomimetics of biologically active metallopeptides
INVENTOR(S): Sharma, Shubh D.; Shi, Yiqun; Rajpurohit, Ramesh; Wu, Zhijun
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013571	A1	20030220	WO 2002-US25574	20020812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2462200	A1	20030220	CA 2002-2462200	20020812
EP 1425029	A1	20040609	EP 2002-768507	20020812
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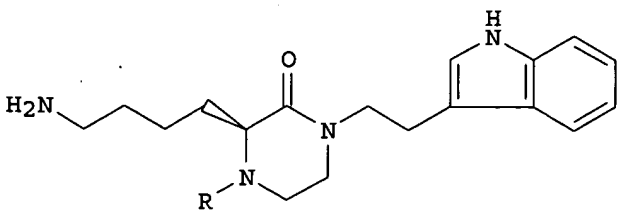
JP 2005504043	T	20050210	JP 2003-518577	20020812
US 2004152134	A1	20040805	US 2004-761889	20040121
US 2004157264	A1	20040812	US 2004-762079	20040121
US 2004167201	A1	20040826	US 2004-776657	20040210
US 2004171520	A1	20040902	US 2004-776419	20040210
US 2005130988	A1	20050616	US 2005-36282	20050114
US 2005124636	A1	20050609	US 2005-40838	20050121
US 2005176728	A1	20050811	US 2005-99814	20050405

PRIORITY APPLN. INFO.:

US 2001-311404P	P	20010810
WO 2002-US25574	W	20020812
US 2003-467442P	P	20030501
US 2003-474497P	P	20030530
US 2004-536606P	P	20040114
US 2004-538100P	P	20040121
US 2004-761889	A2	20040121
US 2004-762079	A2	20040121
US 2004-546393P	P	20040219
US 2004-559741P	P	20040405
US 2004-563739P	P	20040419
US 2004-837519	A2	20040430

OTHER SOURCE(S): MARPAT 138:188071
GI



I

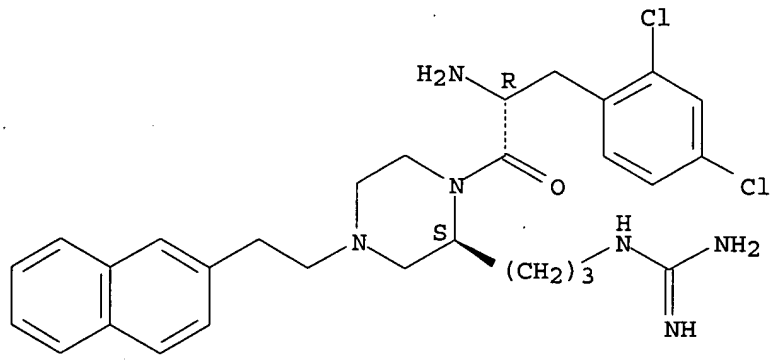
AB The invention relates to a method of deriving a peptidomimetic of a biol. active metallopeptide. The peptidomimetic contains at least one non-peptide ring structure and at least two amino acid-related elements. The invention further relates to peptidomimetics with a template space heterocyclic ring structure, including 5-, 6- and 8-membered and 5-5 and 6-5 bicyclic fused ring structure melanocortin receptor-specific peptidomimetics. The examples describe the synthesis of pyrrolidines, 2-piperazinones [e.g., I [R = BuCH2CH2CO-Ser(Bzl)-D-Phe(2-Cl)]], hexahydropyrrolo[1,2-a]pyrazin-4-ones, hexahydropyrrolo[1,2-a]imidazol-3-ones, 1,4-benzodiazepines, and piperazines. Competitive inhibition testing of compound I against α-MSH yielded the following results at 1 μM: melanocortin-1 receptor (MC1-R) 96%, MC3-R 51%, MC4-R 99%, and MC5-R 82%.

IT 497935-98-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(peptidomimetics of biol. active metallopeptides)

RN 497935-98-5 CAPLUS

CN 2-Piperazinepropanamine, 1-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-N-(aminoiminomethyl)-4-[2-(2-naphthalenyl)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

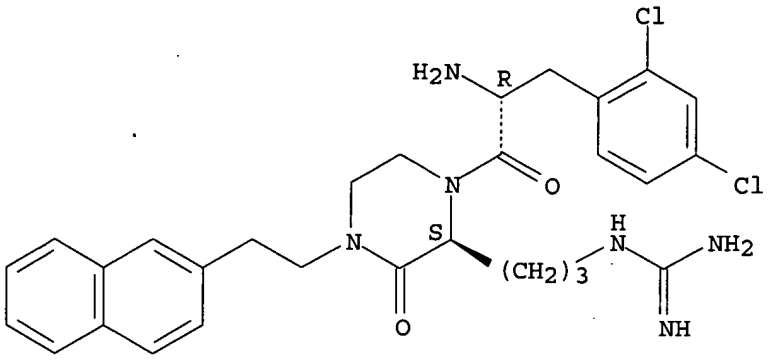


IT 497935-20-3P 497935-41-8P 497935-42-9P
497935-43-0P 497935-44-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetics of biol. active metallopeptides)

RN 497935-20-3 CAPLUS

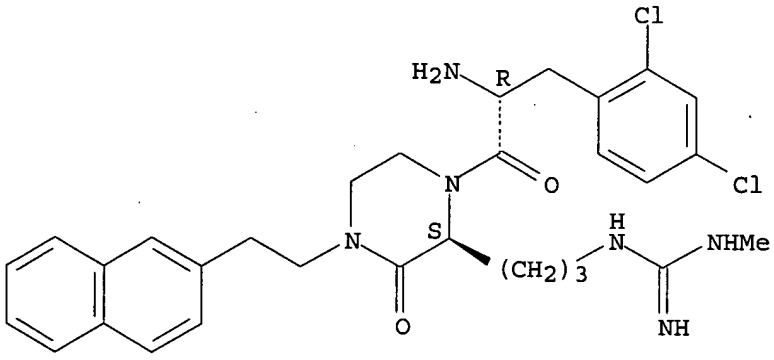
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[(aminoiminomethyl)amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



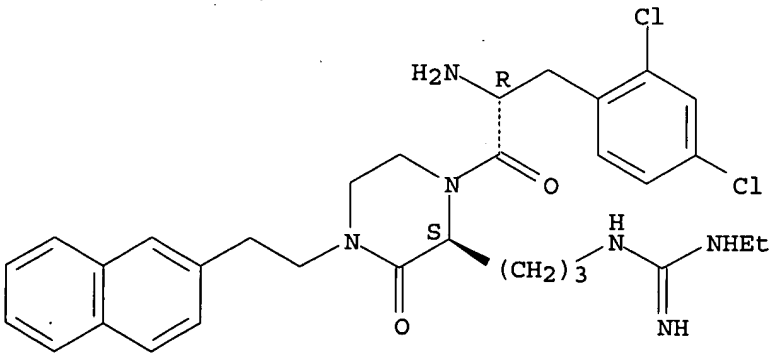
RN 497935-41-8 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(methylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



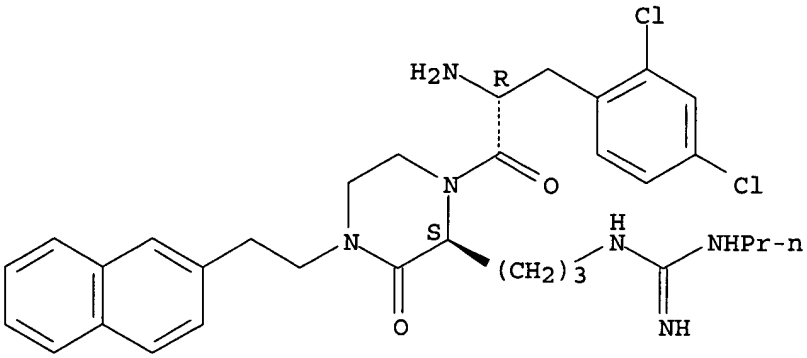
RN 497935-42-9 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[(ethylamino)iminomethyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



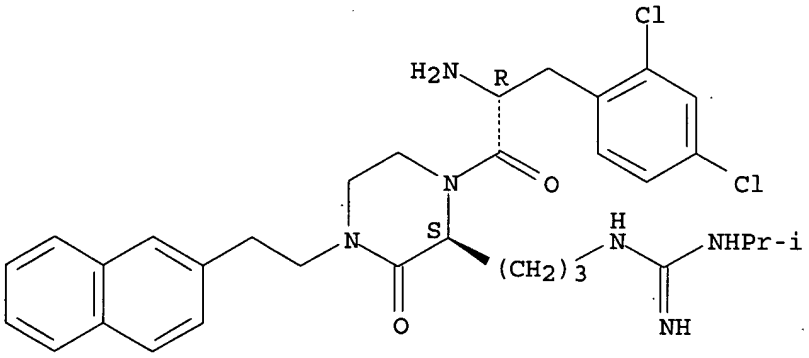
RN 497935-43-0 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino(propylamino)methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 497935-44-1 CAPLUS
CN Piperazinone, 4-[(2R)-2-amino-3-(2,4-dichlorophenyl)-1-oxopropyl]-3-[3-[[imino[(1-methylethyl)amino]methyl]amino]propyl]-1-[2-(2-naphthalenyl)ethyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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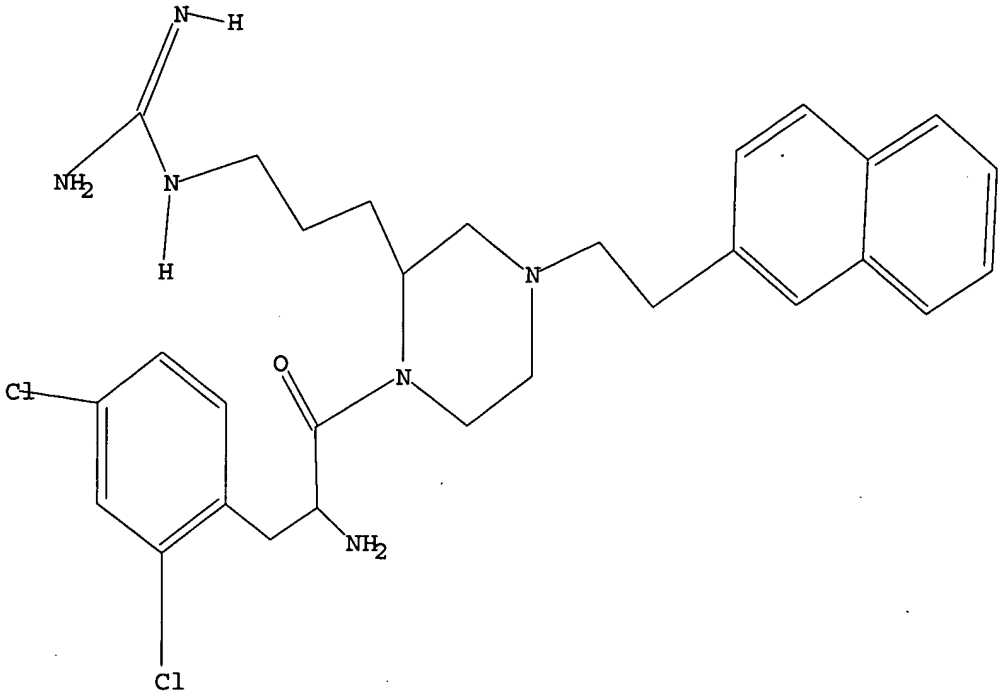
L1 STR



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L2 0 S L1
L3 13 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:01:10 ON 26 JAN 2007
L4 4 S L3

ACCESS DB # 211732

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Mrs Fuller

Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: BEN SACKEY Examiner #: 73487 Date: 01/02/07

Art Unit: 1624 Phone Number: 2-0204 Serial Number: 10/762,079

Location (Bldg/Room#): REM 5B31 (Mailbox #): _____ Results Format Preferred (circle): PAPER DISK

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To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Piperazine melanocortin-specific compounds

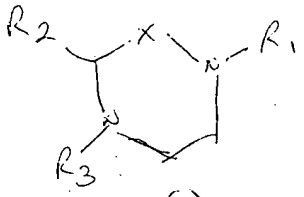
Inventors (please provide full names): Sharma et al.

Earliest Priority Date: 05/30/03

Search Topic:

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



(1)

R^1, R^2 and R^3 are as defined

L_2 linker is as defined in claim 1

L_1 linker is as defined in claim 1.

Thanks